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With International Abstract of Surgery

VOLUME 77 November, 1943 NUMBER 5

The Newer Concepts of Meat in Nutrition

Meat...

and the "Psychic Factor" in Adequate Nutrition

EVER since Pavlov so conclusively demonstrated the "cephalic phase" of digestion, the profound provocative influence of the sight and smell of well prepared, attractive food has been placed on a scientific plane. Through the visual and olfactory senses, a chain of reflexes is set in motion, which increase the flow of digestive juices and augment gastric motility. The appetite is whetted, the satiety value of the meal is enhanced, and digestion is improved.

Meat has long been recognized for its properties of stimulating the appetite. The aroma of well cooked meat, due to its extractives, prepares the digestive tract for the reception of the meal about to be eaten. The taste of the extractives adds further to this favorable reaction.

Because of these desirable properties meat now plays a new and important role in wartime meal planning. Food restrictions necessitate the use of a greater proportion of carbohydrate foods. By properly combining meat with other foods, the taste appeal of the latter is enhanced, and the meal as a whole becomes more tasty and satisfying. The current weekly food ration is quite adequate for the preparation of one or two meat containing meals daily, especially if the variety meats and poultry are employed. Thus no meal need lose in its palate appeal, nor need it be less attractive than when meat was more generously available.

This feature of meat is present in all cuts, including those of lower point value. Also provided by all kinds and cuts of meat are biologically adequate protein, essential minerals, and the B vitamins thiamine, riboflavin, and niacin. Meat therefore not only encourages the consumption of many non-rationed foods, but also complements them so as to enhance their nutritional value.

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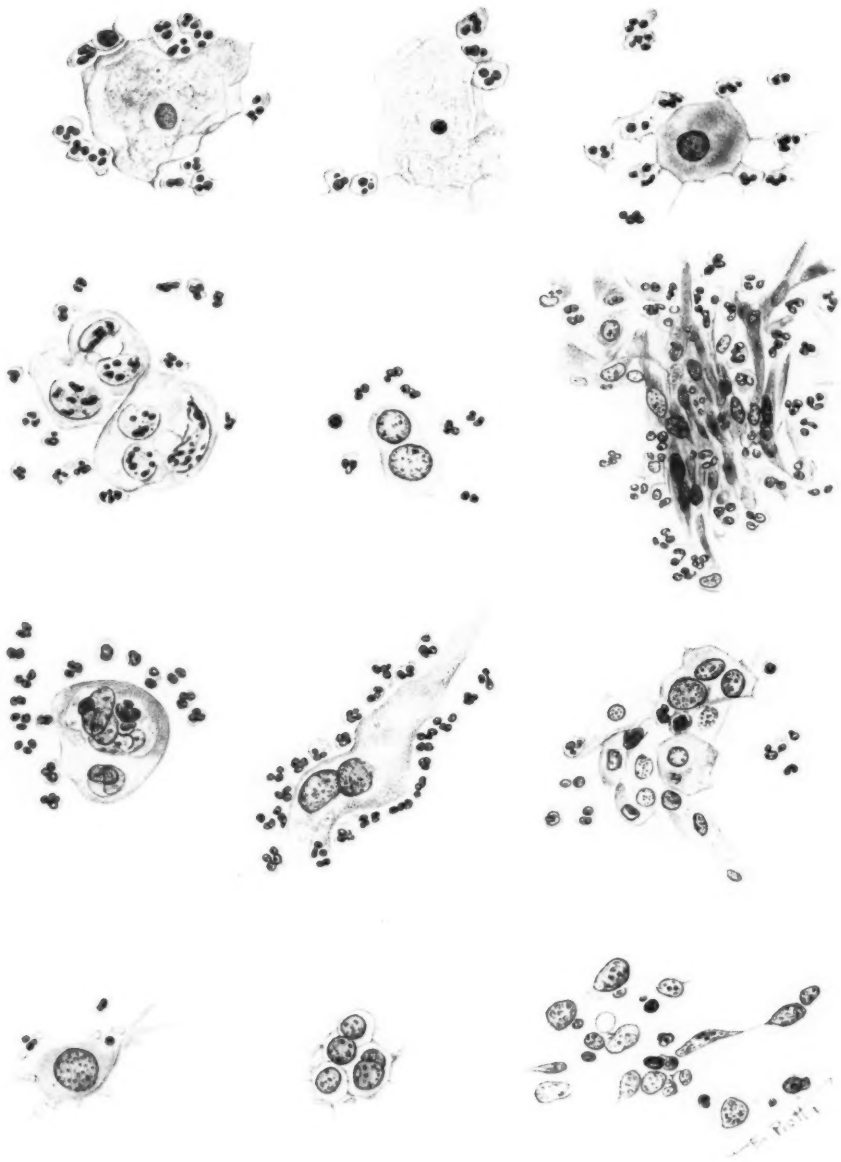

The Value of the Vaginal Smear in the Diagnosis of Uterine Cancer.—Joe Vincent Meigs, Ruth M. Graham, Maurice Fremont-Smith, Israel Kapnick, and Rulon W. Rawson

UNIV. OF MICH.

SURGERY

GYNECOLOGY AND OBSTETRICS

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THE VALUE OF THE VAGINAL SMEAR IN THE DIAGNOSIS OF UTERINE CANCER

JOE VINCENT MEIGS, M.D., F.A.C.S., RUTH M. GRAHAM, B.S., MAURICE FREMONT-SMITH, M.D., F.A.C.P., ISRAEL KAPNICK, M.D., and RULON W. RAWSON, M.D., Boston, Massachusetts

CANCER of the cervix and body of the uterus is a curable condition (1, 8). Early diagnosis and treatment are prerequisites for cure. Bigelow and Lombard say that in certain forms of cancer the chance of cure decreases 4 per cent a week. Approximately the same statement is given for carcinoma of the cervix by Todd who reports that from the onset of abnormal bleeding the chance of cure decreases 3.34 per cent a week. The average time from the onset of symptoms to operation is stated to be 7.5 months (2, 7, 17). Eleven of a hundred women with cancer of the cervix reach the surgeon in the early (operable) stage; 29 in the stage of so called "border-line operability"; 60 are totally inoperable when treatment is begun (8).

Delay is thus responsible for a majority of deaths from cervical cancer, a delay to which both patient and physician contribute. A patient with cancer of the cervix reports to her physician on the average 4 months after the onset of bleeding; from the patient's first visit another 4 months intervene before operation is performed. Figures quoted by Simmons and Daland in 1924 and by Hoge in 1942 are almost identical as to preoperative time wasted.

The critical weeks lost by the patient can be salvaged only by slow education of the public. We are concerned here with the fact that the physician, confronted by early cancer of the cervix or endometrium, often fails to make a diagnosis during the only period when the life of the patient can be saved. Ignorance, desire

From the Vincent Memorial Hospital (the Gynecologic Service of the Massachusetts General Hospital), the Pondville Hospital (Massachusetts Department of Public Health), and the Thyroid Laboratory of the Massachusetts General Hospital.

From the Departments of Gynecology and Medicine of the Harvard Medical School.

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(*Legends for frontispiece.*)

First row, normal cells. Reading from left to right: normal precornified cell with basophilic cytoplasm and vesicular nucleus; normal fully cornified cell with acidophilic cytoplasm and pyknotic nucleus; normal basal cell with large vesicular nucleus. (Magnification×875.)

Second row, cells seen in carcinoma of the cervix. Reading from left to right: large atypical histiocytes with phagocytosed material and vacuoles; two cells with large nuclei (note especially size of nucleus in relation to size of cell); group of "fiber-like" cells with elongated nuclei showing considerable variation in size. (Magnification×875.)

Third row, cells seen in carcinoma of the cervix. Reading from left to right: large multinucleated giant cells; "tadpole" cell with double nucleus; group of atypical cells with variation in size and shape of nucleus. (Magnification×875.)

Fourth row, cells seen in carcinoma of the endometrium. Reading from left to right: large cell with large vesicular nucleus; group of abnormal cells with significant variation in size and shape of nucleus; atypical cells smeared from tumor in carcinoma of endometrium. (Magnification×875.)

to give reassurance, unfamiliarity with pelvic examination, reluctance to advise biopsy, ether examination and curettage all contribute to the critical delay. A technically simple method of making a presumptive diagnosis of uterine cancer in daily office practice would aid greatly in the early discovery of female genital malignancy. Such a method has been described by Papanicolaou (11,12,13) by which a diagnosis of uterine carcinoma may be made by examination of the vaginal smear. By suitable collection, fixing, and staining of the vaginal secretion he has been able to identify cells present only in malignancy of the female genital tract.

In the belief that this work, if corroborated, places in the hands of the practitioner a practical method of early diagnosis, we have studied the vaginal smears taken from 220 patients.

MATERIAL

The material for this study comes from two sources: one, the Vincent Memorial Wards of the Massachusetts General Hospital and the Gynecologic Tumor Clinic, and the private practices of those associated with these two services; two, the Gynecologic Service of the Pondville Hospital (Massachusetts Department of Public Health) and its Gynecologic and General Surgical Out-Patient Clinics. One hundred and fifty-seven cases were taken from the Massachusetts General Clinic and 63 from the Pondville Hospital. These two sources are rich in material—the Massachusetts General Hospital having many gynecologic patients with nonmalignant lesions, and the Pondville Hospital having many with malignant lesions. The vaginal smears in all instances were taken by the authors themselves. Two of the authors, R. G. and I. K., made independent observations upon each slide of the Pondville series. In most cases the result of the biopsy was not known to either examiner. All smears were called either positive or negative, none "suspicious." It is noteworthy, as an indication of the specificity of this method that in no instance was there disagreement between the two examiners.

TECHNIQUE

The technique for taking vaginal smears is that described by Papanicolaou (11). A slightly curved glass pipette, 8 inches in length is attached to a 3 inch rubber suction bulb. The pipette must be absolutely dry and the patient must not have douched the same day. These precautions are necessary since water in the vaginal smear destroys the cellular detail. The rubber bulb is compressed and the pipette is then inserted into the vagina as far as possible in order to reach the fornix. The bulb is released, and the pipette withdrawn slowly. The material is blown on a previously marked slide which is immediately dropped into a bottle of fixative (one half ether and one half 95% alcohol). Since drying destroys cellular detail it is essential that the slide be placed immediately in the fixative. Fixation for 5 minutes is sufficient, but slides may be left in the fixative without deterioration for as long as 2 weeks.

The slides are run down through the alcohols (70%, 50%) to distilled water. They are stained for 3 minutes in Harris hematoxylin, dipped four times in a 0.5 per cent solution of hydrochloric acid, washed in running tap water, and placed in a 0.5 per cent solution of lithium carbonate for 1 minute. The slides are washed again in running tap water, rinsed in distilled water, and run up through the alcohols (50%, 70%, 80%) to 95 per cent alcohol. They are then stained for 1 minute in a 0.5 per cent solution of orange G in 95 per cent alcohol. The smears are next washed in two changes of 95 per cent alcohol. They are stained in EA 36[1] for 2 minutes, washed in three changes of 95 per cent alcohol, run through absolute alcohol to xylol, and mounted in Canada balsam (10).

DIAGNOSTIC CRITERIA

To recognize the atypical cells found in carcinoma of the cervix and endometrium it is necessary at the outset to know the *normal cells* of the vaginal secretion. These normal cells may be divided into three groups: the cornified series, the basal cells, and the endometrial cells. Cornified cells are again divided in two groups, precornified and fully cornified. The precornified cells are large wafer-like cells with abundant thin green cytoplasm and a

[1] EA 36 consists of:

Light green S. F. yellowish	0.5% in 95% alcohol	45 c.c.
Bismarck brown	0.5% in 95% alcohol	10 c.c.
Eosin yellowish	0.5% in 95% alcohol	45 c.c.
Acid phosphotungstic		0.200 gram
Lithium carbonate, saturated aqueous solution		1 drop

vesicular nucleus (Fig. 1). The fully cornified cells are similar to the precornified with the exception that the cytoplasm stains pink and the nucleus is pyknotic. The cytoplasm may show some signs of degeneration such as wrinkling and granulation (Fig. 1). Basal cells are smaller, round or oval cells with green cytoplasm and a vesicular nucleus (Fig. 2). With extreme atrophy of the genital tract the nuclei of the normal basal cells may contain chromatin in large clumps. Endometrial cells are the smallest of the normal cells. They consist of a small vesicular nucleus with very little cytoplasm. They show little variation in size and shape (Fig. 3).

The criteria for the diagnosis of *carcinoma of the cervix* are as follows: the cells show great variation in size, shape, and form — much greater variation than is usually seen in the pathological section of the same tumor. The most striking variation in shape appears in the tremendously elongated "tadpole" cells (Fig. 4), which have a rounded head containing the nucleus and a long thin tail. Long fiber-like cells may be found (Fig. 5). These cells are extremely elongated, with tapered ends, and contain an elongated nucleus, or two or three nuclei. They may be found singly or in groups.

Many atypical cells have vacuolated cytoplasm giving the cell a foamy appearance, but cellular vacuolization is not diagnostic of malignancy. Staining characteristics of the cytoplasm are not diagnostic, since in the vaginal smear the atypical cells may have either basophilic or acidophilic cytoplasm. This variation in staining may be due to differences in the acidity of the vagina as the result of either infection, parasitic infestation, or estrogen elaboration.

The nuclei of abnormal cells show marked variation in shape and size, and bizarre forms occur. There are often signs of increased activity of the nuclei, as indicated by clumping of the chromatin, granularity of the nucleus, and occasionally an apparent increase in the amount of nuclear material. Nucleoli are seen occasionally but not consistently enough to make observation of the nucleolus an important aid in diagnosis. Mitoses may occur but are very rare. However, cells are seen which appear to be in a preliminary stage of mitosis. The most frequent variation of the nucleus is its size. In the abnormal cell the nucleus often fills the entire cell, leaving a thin, but distinct rim of cytoplasm (Fig. 6). Often multinucleated giant cells are seen, occasionally containing as many as a dozen nuclei (Fig. 7).

Histiocytes are often present in positive smears (Fig. 8). The histiocytes vary greatly in size. They often contain phagocytosed cellular elements such as red blood cells, leucocytes, and cellular débris. They frequently have acidophilic cytoplasm. The histiocytes continue to show numerous vacuoles even after ingestion of cellular elements. Histiocytes may appear in normal smears.

Leucocytes are usually present, but their numbers vary tremendously. In an occasional positive smear they appear in clumps.

Red blood cells or evidence of old bleeding are present in every positive smear. We have never made a diagnosis of malignancy without some evidence of blood. The evidence of bleeding may be either red blood cells (which occasionally stain basophilic), fibrin, or old blood pigment, which appears as small orange or green, fern-like deposits.

In the diagnosis of *endometrial cancer* the same general criteria apply: evidence of blood must be present; an increase in leucocytes is usually seen; histiocytes are frequently found. The variation in size of individual atypical cells in endometrial cancer is not so great as in cervical. The cells are more like those seen in stained sections of the same tumor. Abnormal endometrial cells are usually found in clumps which can be easily seen under low power. These cells show very little cytoplasm and the nuclei are usually hyperchromic. The chromatin may appear as dark granules in the nuclei. The nuclei vary tremendously in size. We have found that the diameter of normal endometrial nuclei varies between 3.7 micra and 9.4 micra. The nuclei of tumor cells were found to measure 2.8 to 14.1 micra. Haumeder found the nuclei of cells in carcinoma of the endometrium to be twice as large as those found in hyperplasia of the endometrium. Occasionally in endometrial carcinoma large cells are seen with an abundant amount of cytoplasm and large vesicular nuclei (Fig. 9), but are rare. Mitoses (Fig. 10) are very rare.

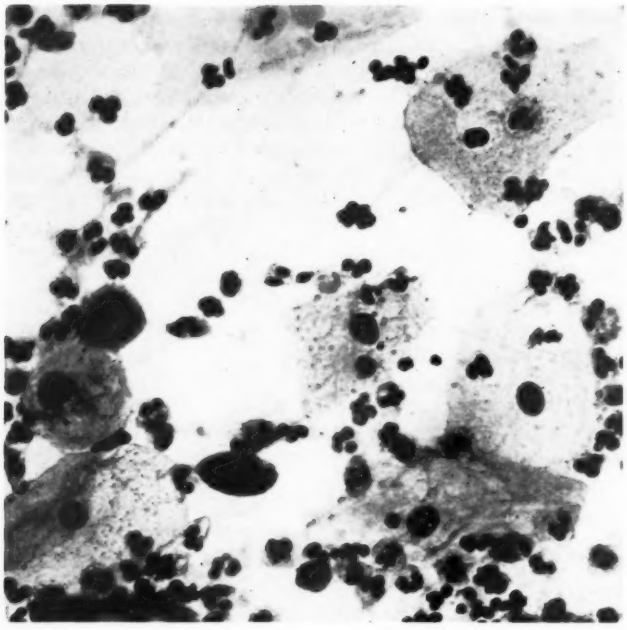

Fig. 1. Negative smear showing cornified and precornified cells, and two basal cells in lower left hand corner. Magnification×825.

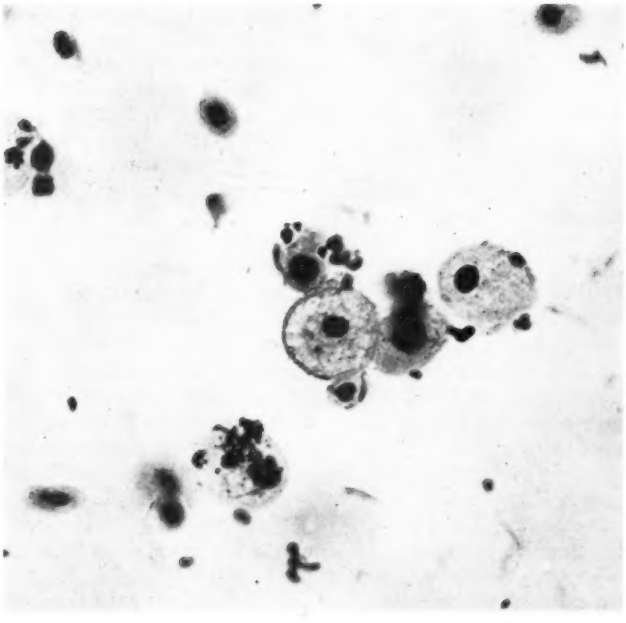

Fig. 2. Negative atrophic smear showing a field of basal cells. Magnification ×825.

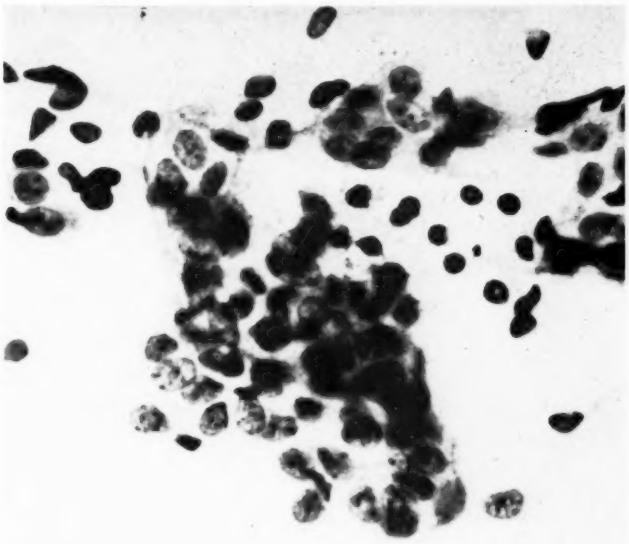

Fig. 3. Smear taken from normal endometrium after surgical removal of the uterus. Compare with Figure 12. Magnification×825.

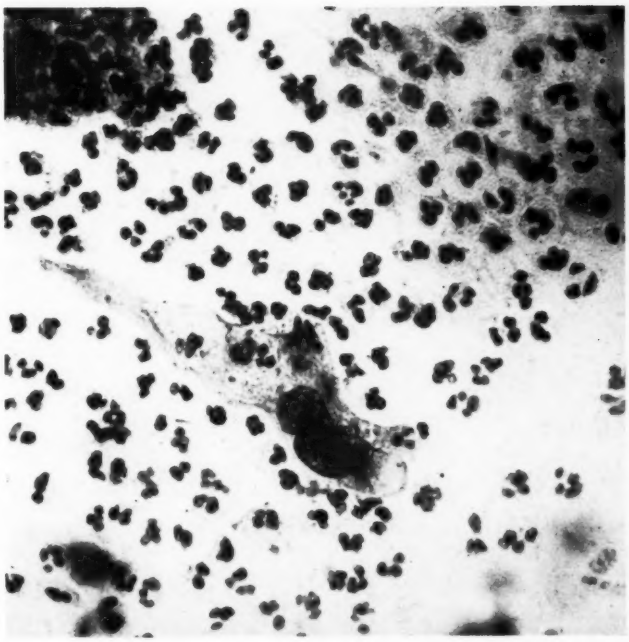

Fig. 4. Carcinoma of the cervix. A huge bizarre shaped cell with double nuclei illustrating the marked variation in size and shape of cells encountered in carcinoma of the cervix. (Tadpole cell.) Magnification×825.

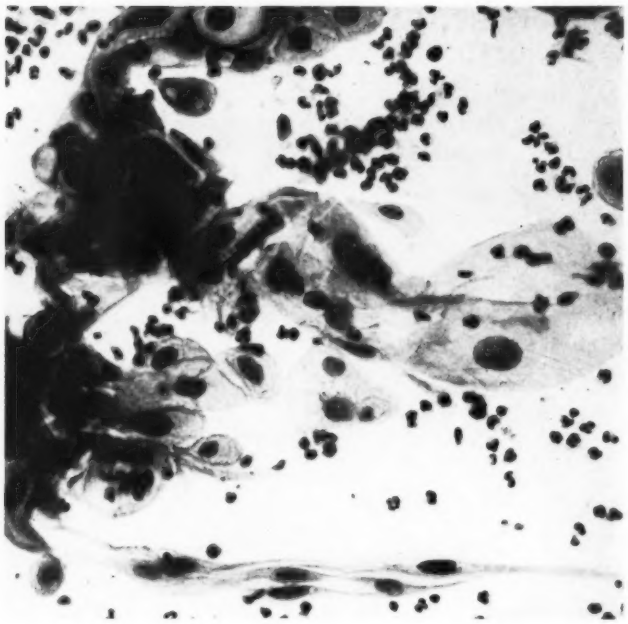

Fig. 5. A group of atypical cells seen in epidermoid cervical cancer. The long fiber-like cells in the lower portion of the photomicrograph are abnormal cells encountered frequently in positive smears. Magnification×825.

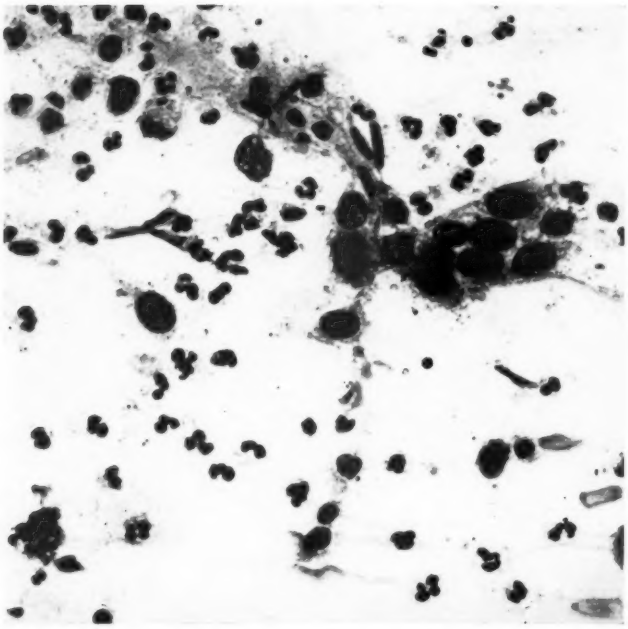

Fig. 6. Atypical cell group seen in epidermoid carcinoma of the cervix, illustrating the abnormal variation in size and shape of the nuclei. Magnification×825.

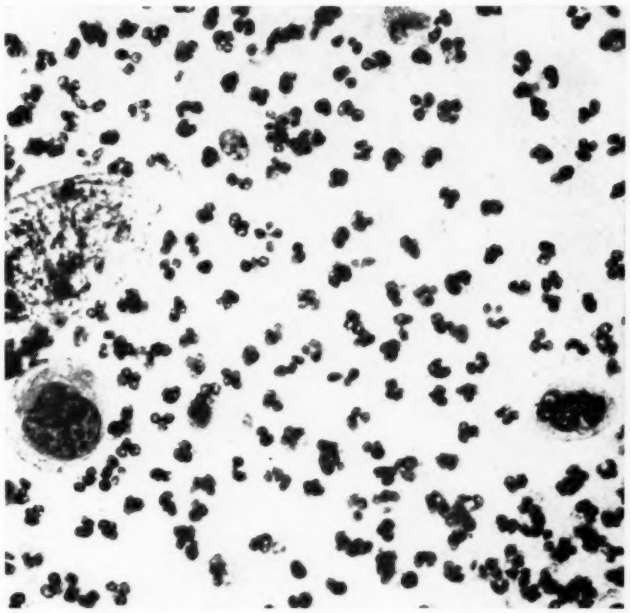

Fig. 7. Two multinucleated giant cells seen in epidermoid carcinoma of the cervix. Magnification×825.

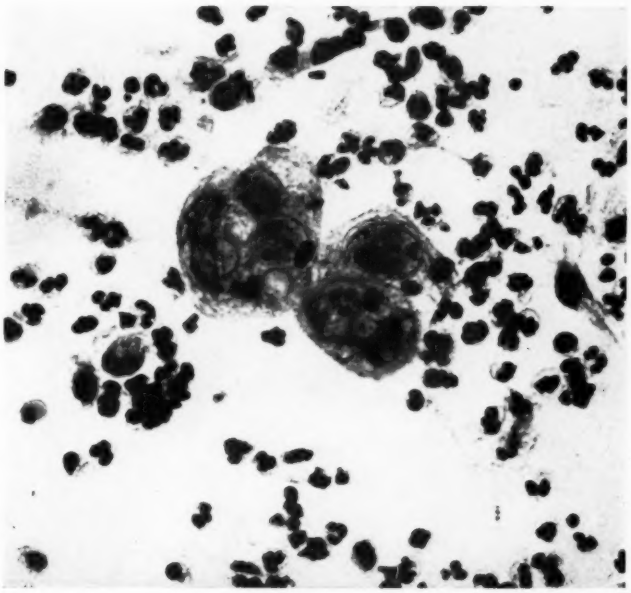

Fig. 8. Two large histiocytes with phagocytosed polymorphonuclear leucocytes and red blood cells seen in a vaginal smear from a case of epidermoid cervical cancer. Magnification×825.

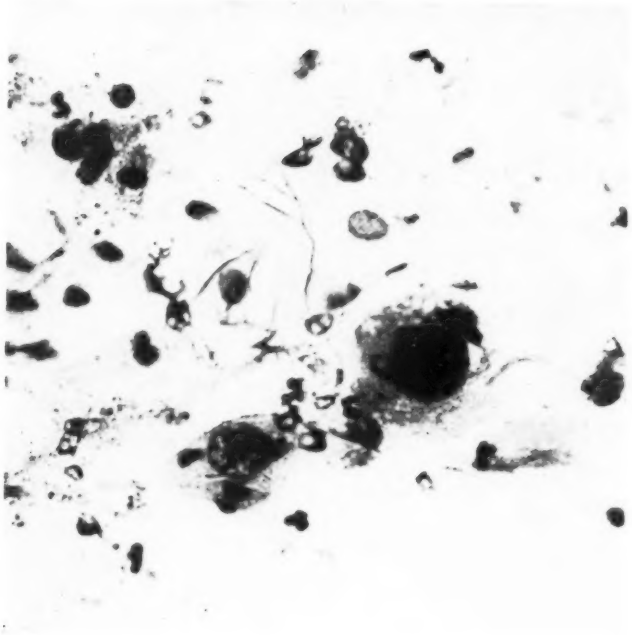

Fig. 9. Adenocarcinoma of the endometrium. Atypical large cells with huge vesicular nuclei—a rare type of cell seen in endometrial carcinoma. Magnification ×825.

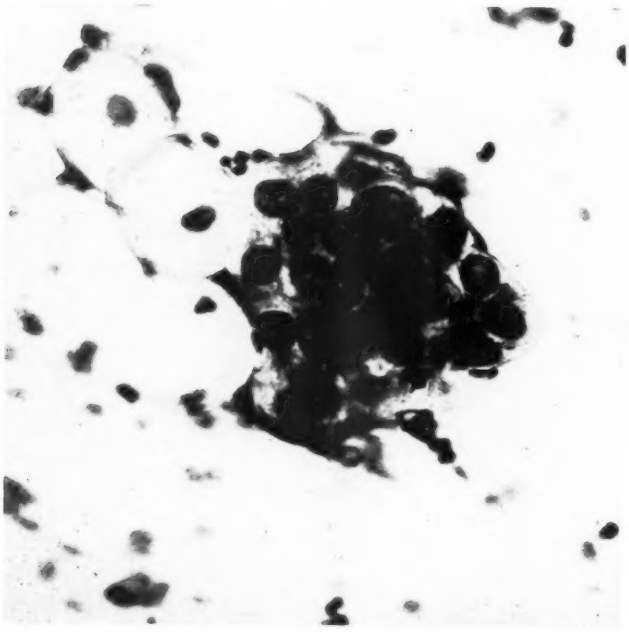

Fig. 10. Adenocarcinoma of the endometrium, group of cancer cells. One cell is in mitosis. Magnification ×825.

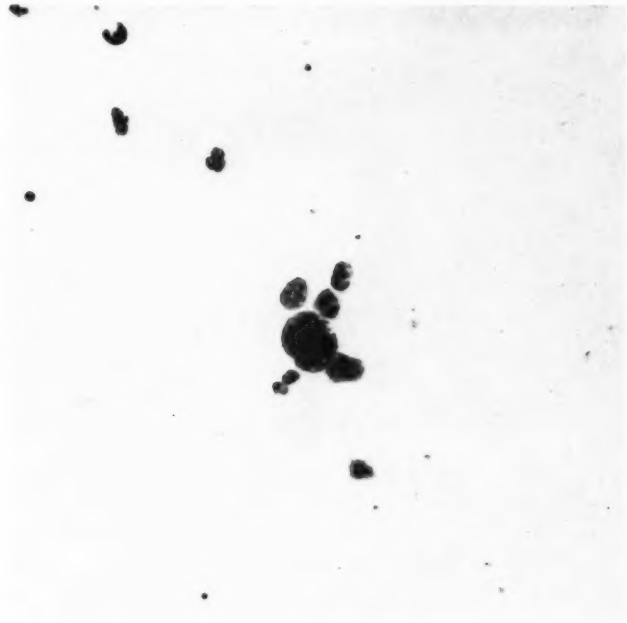

Fig. 11. Adenocarcinoma of the endometrium. Atypical cells showing great variation in size and vesicular nuclei with no apparent cytoplasm. Vaginal smear. Magnification ×825.

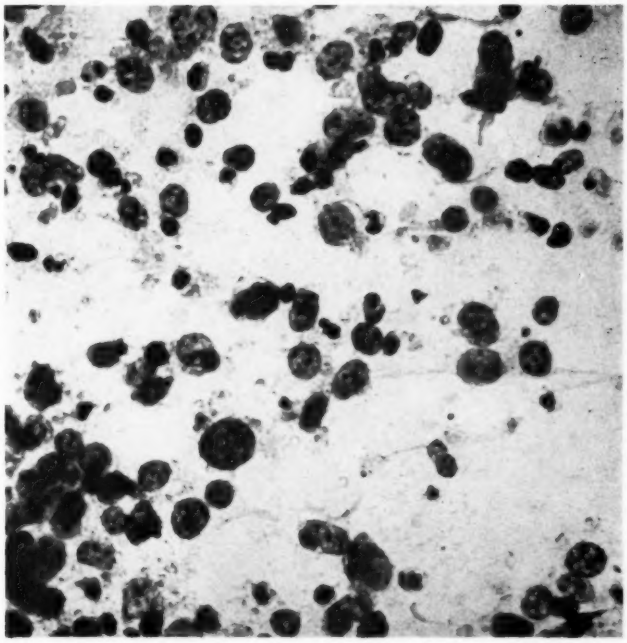

Fig. 12. Same case as smear in Fig. 11. Smear taken from the tumor showing the same type of cells as were found in the vaginal smear. Magnification ×825.

Fig. 13. Epidermoid carcinoma of the cervix. Atypical cells found in the vaginal smear. Magnification×825.

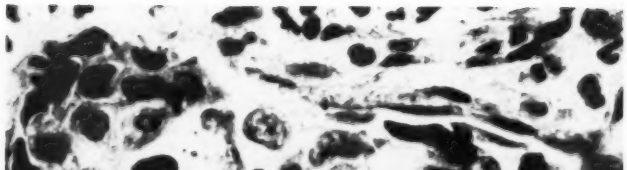

Fig. 14. Histiological section of the same tumor (Fig. 13), showing the same type of cells. Magnification×825.

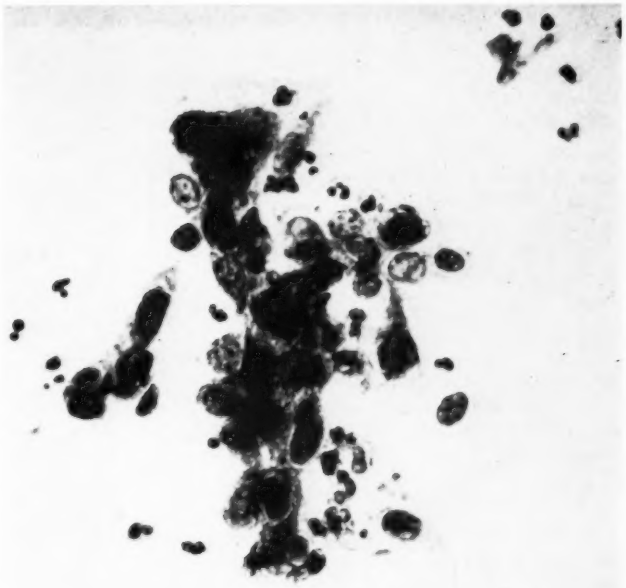

Fig. 15. Same case as in Figure 13. Similar atypical cell seen in smear from tumor. Magnification×825.

In some smears the tumor cells are so abnormal that they are easily recognized and the diagnosis is made without difficulty. In other positive cases, the variation from the normal is not so apparent and the diagnosis can be made only after long and careful study has been carried out.

An attempt was made to determine whether the abnormal cells seen in the vaginal smear were actually tumor cells, or whether they represented a tissue reaction secondary to the presence of cancer. Smears were therefore taken from the tumor as soon as it was removed at operation. By taking the smears with a pipette the conditions of the vaginal smear were approximated. Smears were taken from the tumor in 7 cases of cervical cancer and in 3 cases of endometrial cancer. In each case the same type of cell found in the vaginal secretion was found in the smear from the tumor itself (Figs. 11 and 12; Figs. 13, 14, 15). These observations are presumptive evidence, since the cytology is the same in both cases, that the abnormal cells seen in the vaginal smears are actual tumor cells.

RESULTS

With the methods described we have studied one or more vaginal smears in 220 cases. No cancer cells were found in smears taken from 153 women. Smears were taken from these patients because they were either in the cancer age or because of symptoms of vaginal bleeding or discharge. Of these, 79 had biopsies, curettage, or hysterectomy with negative tissue diagnosis for cancer. The remainder of these patients with negative smears did not present enough evidence for malignant disease to require operative procedures.

A histological diagnosis of uterine carcinoma was made in 62 cases. Forty-six of these patients were found to have carcinoma of the cervix. Forty of these cancers were epidermoid. There were 3 each of adenocarcinoma and adenoacanthoma. Of the 46 cases with proved cancer of the cervix, positive vaginal smear diagnoses were made in 45—percentage error of 2.2. Ten cases, or 22 per cent, were classified as early (1A) cervical carcinoma.

Twelve cases had endometrial cancer. Ten adenocarcinomas and two adenoacanthomas

were found. Five were classified as early cancer. Of the 12 cases with endometrial cancer 11 were diagnosed with vaginal smear—percentage error of 8.3.

Epidermoid cancer of the vagina was found in 3 patients whose vaginal smears were positive. Cancer cells were found in the vaginal smear taken from 1 patient who had a cancer of the rectum and a rectovaginal fistula. In view of negative pathological findings on examination of the uterine curettements we concluded that the tumor cells probably came from the rectal cancer.

Of 153 negative cases positive smears were reported in 4—error 2.6 per cent.

Vaginal smears diagnosed as positive were taken from 5 patients who have not yet come to operation. They are classified as incomplete.

EVALUATION OF STUDY

There have been many attempts to diagnose cancer from single cells or groups of cells. The majority of these studies deal primarily with the cells found in pleural and ascitic fluid. In early studies the fluid was smeared on a slide, fixed, stained, and examined. Gradually this method was replaced by centrifuging the fluid, fixing the sediment, imbedding in paraffin, cutting and staining. McDonald and Broders believe that smears are as satisfactory as the centrifuged fixed specimen. They publish no statistics. Zemansky using the fixed centrifuged specimen gives statistics on the method in pleural and ascitic fluids. In cases with malignant disease he reports 54 per cent diagnosed accurately. Foot using the same method found that carcinoma could be correctly diagnosed in 69 per cent of abdominal fluids, and in 31 per cent of thoracic fluids. Foot believes that in a diagnosis of cancer the most important criterion is the ratio between the nucleus and nucleolus. Quinsel also emphasizes the importance of the size of the nucleolus. Schlesinger used as criteria of malignancy groups of cells showing polarity, sharply distinct cell walls, and acinar or pseudoacinar formation. He reports 60 per cent accuracy of diagnosis. Graham stresses the importance of true tumor giant cells in serous effusions.

Recently Gowar has published results on the examination of the sputum in carcinoma of the lung. An accurate diagnosis was made in 64.3 per cent of positive cases. As criteria of malignancy he lists abnormalities in size and shape of nucleus, the presence of nuclei often containing more than one nucleolus, and multinucleated giant cells.

As early as 1928 Papanicolaou recognized cancer cells in the vaginal smear. Papanicolaou and Traut (13) in their recent monograph report that they failed to detect malignant cells in 4 of a total of 127 cases with demonstrable cancer of the cervix. They found cancer cells in the vaginal smears of 46 of 53 patients with cancer of the fundus. Our results and those of Papanicolaou indicate that a cancer cell can be more readily identified in the vaginal smear than in body fluid sediments or sputa. This increased accuracy in diagnosis is probably due to the fact that the cells in the vaginal fluid are in greater concentration and have suffered less degeneration.

In considering the mistakes that we have made in diagnosis there are certain important lessons to be learned. Two cases with proved cancer had negative vaginal smears. In each instance only one smear was available for study. It is therefore evident that in any clinically suspicious case one negative smear cannot be depended upon to exclude the presence of cancer. We do not know how many negative smears are needed to prove that cancer is not present. Sixteen smears were taken over a period of 7 days from 1 patient with cervical cancer. Cancer cells appeared in 6 smears only.

In 3 cases cancer was indicated by the smear, but curettage proved negative. Hysterectomy was not performed. These patients are being carefully followed. In another case the smear was positive. No cancer was found on routine pathological examination after complete removal of the uterus. No serial sections were done and the specimen was discarded by the laboratory.

These mistakes should be considered in relation to the following cases.

M.E., P.C. No. 9386. A single woman, aged 69 years, was seen on January 18, 1943. Six months before she had noticed vaginal bleeding, and for 1 month she had a colorless vaginal discharge. The uterus was forward, small and movable. Curettings revealed a polypoid area on the posterior wall of the uterus. The pathologist reported adenoacanthoma

of the uterus. Before operation a vaginal smear was taken. The uterus, cervix, tubes, and ovaries were removed by total abdominal hysterectomy. The vaginal smear was positive and the report from the pathology laboratory showed fibroids, cervical polyp, multiple follicular cysts of the ovary, stromal hyperplasia of the ovary, but *no cancer*.

This case is one of very early adenoacanthoma (adenosquamous cancer) with positive biopsy and positive vaginal smear, but the laboratory found no evidence of cancer on routine section of the excised uterus. The blocks were discarded and could not be recut.

D.Y., P.C. No. 9511. A married woman aged 49 years, with no children, was seen on February 24, 1943, complaining of a discharge since 1931. Three years ago with the menopause the discharge decreased until August, 1942, when it became more profuse and colored. Examination showed a clean cervix with a few exposed cervical ducts. The uterus was forward, of normal size, and movable. There was a mass in the right vault. A vaginal smear was taken and an endometrial biopsy was done. The smear and the biopsy were both positive for endometrial cancer. On March 5, 1943, another smear was taken and was positive. The uterus was removed by means of total abdominal hysterectomy and on examination of the gross specimen the endometrium suggested cancer. About 15 sections of the endometrium were cut and no cancer was found. Blocks were then re-cut, 50 more sections were made, and in 2 sections adenocarcinoma was found. The diagnosis was confirmed by Dr. Tracy B. Mallory.

These two cases illustrate that failure to demonstrate cancer on routine pathological examination of the excised specimen does not exclude the presence of cancer. The proof rests upon a negative result following complete serial section of the uterus.

It should be noted that in both these cases in which a positive diagnosis was made by vaginal smear the cancer was in an early stage. To date we have made and confirmed the diagnosis of cancer in 15 early cases.

An example of early cervical cancer diagnosed by the vaginal smear technique follows.

Mrs. H. W. H., P. H. No. 21070, a 43 year old woman, entered the clinic complaining of 1 month's intermenstrual spotting. The cervix presented an erosion of the left anterior lip at the external os. Biopsy revealed chronic cervicitis. No vaginal smear was done. Two months later a small, nonulcerated, hard, nodular area was found in the anterior portion of the left lateral lip. Vaginal smears were positive. After a positive biopsy a Wertheim hysterectomy was done. The cancer measured 1.5 by 1.0 centimeters.

We do not feel justified in advising operation for uterine cancer solely on the evidence of a positive vaginal smear. The positive smears should be confirmed by biopsy or curettage. This method is comparable to tuberculin testing of college students for tuberculosis, who are thereby screened, chest x-ray films being indicated only in the positive reactors.

In our hands this method of diagnosis has proved of significant value. A systematic study of the entire smear and an experienced knowledge of cytology are necessary in this type of examination. We advise incorporation of this method of diagnosis as a part of every routine physical examination in office, outpatient department, and hospital. It is possible that State cancer diagnostic laboratories should make vaginal smear diagnostic service available to the physicians of the community.

SUMMARY

We have studied vaginal smears from 220 women in an attempt to make the diagnosis of uterine cancer. The technique, criteria for diagnosis of cancer, and accuracy of diagnosis have been discussed. We believe that by vaginal smear examination uterine cancer can be diagnosed in an early stage.

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SURGICAL TREATMENT OF ACQUIRED ANEURYSM AND ARTERIOVENOUS FISTULA OF PERIPHERAL VESSELS

Review of Sixty-Seven Cases

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FOR centuries attempts have been made to cure aneurysms of peripheral vessels by surgical methods. Prior to the time of Matas, the classical method of Antyllus and that of Purmann were available for the radical cure of the condition and Hunterian ligation was practiced widely because of the dangers inherent in the direct surgical attack on the aneurysm. Matas performed the first endoaneurysmorrhaphy in March, 1888, and his work during the next few years (11), with that of Halsted, led to the modern development of surgery of aneurysms of peripheral vessels.

Arteriovenous fistula was recognized first by William Hunter in 1757. Breschet, in 1833, according to Holman (9), attempted in 2 cases to cure the condition surgically by proximal ligation of the artery but gangrene ensued in both cases. Norris, in 1843, reported the first surgical cure, which was achieved by proximal and distal ligation of the artery. By 1886, Bramann was able to conclude, from a review of 159 cases of arteriovenous fistula, that Hunterian ligation was to be condemned absolutely and that the treatment of choice was quadruple ligation and excision or obliteration of the communication between the artery and the vein. Matas' methods of endoaneurysmorrhaphy were applied in the treatment of arteriovenous aneurysm by Bickham in 1904. More recently the many observations and contributions of Makins, Matas (11, 12, 13), Holman (7, 8, 9), Reid (20, 21, 22) and others have clarified the pathological physiology of arteriovenous fistula.

The present review is based on the records of a series of 67 patients who suffered from acquired peripheral aneurysm or arteriovenous fistula or both and who were treated by operation at the clinic. Several cases of lesions that involved the great vessels leading to the extremities have been included. It was our purpose in reviewing the records of the cases to determine, in particular, which operative procedures have been employed and the results following the several different procedures. While acquired arterial aneurysm and arteriovenous fistulas may differ markedly in their causation and symptoms and in the methods necessary for their correction, the two types of lesions are similar in that their radical cure often demands that the main arterial supply of the extremity be interrupted. In either case, a careful evaluation of the collateral circulation must be made before operation is undertaken.

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SIGNS AND SYMPTOMS

The signs and symptoms of peripheral aneurysm and arteriovenous fistula are well known, and usually are so typical that the diagnosis may be made with certainty. In the case of aneurysm, the characteristic expansile, pulsating tumor situated along the course of a vessel and associated with a systolic bruit and thrill is pathognomonic. Some confusion may arise when the aneurysm is more deep seated or is surrounded by inflammatory thickening of extravasated blood. Interference with the arterial supply to the limb, venous stasis with edema, claudication and ischemic neuritis are often present.

Local, regional and systemic effects are produced by an arteriovenous fistula. One of us (Pemberton) and Saint proposed that the local effects be considered those shown by the involved vessels, the regional effects those manifest in the involved limb, and the systemic effects those shown by the general circulatory system. The involved vein shows dilatation, tortuosity, and elongation while the artery

proximal to the fistula shows dilatation, thinning, and degeneration in all its coats. The involved limb shows hypertrophy, an increased temperature, and trophic effects, which are due to decreased capillary blood flow and to the impeded venous return. The systemic effects, as shown by Holman (8), depend on the size of the fistula and on the unobstructed return flow of blood to the heart. The larger the fistula and the longer it exists, the more likely are cardiovascular changes to develop. These changes are explicable on physiological grounds and depend primarily on an increase of the total volume of the circulating blood per unit of time and particularly on the volume flowing through the circuit of heart, artery, fistula, and vein. The cardiac hypertrophy is a result of the increased work necessary to handle the increased blood flowing through the heart per unit of time, while the dilatation of the heart is part of the general dilatation of the vessels necessary to handle the increased volume of blood flowing through the circuit of the heart, artery, fistula, and vein (7).

In addition to the pulsating, expansile mass and the engorged and often pulsating veins, the continuous bruit and thrill with systolic amplification and the increased beat in the region of the fistula are usually so unmistakable that aneurysm and arteriovenous fistula are not confused. Rarely, studies of the carbon dioxide and oxygen content of blood taken from a vein near the lesion are necessary to distinguish definitely between the two conditions. The transient rise and fall of blood pressure and fall of pulse rate (Branham's bradycardic reaction) when an arteriovenous fistula or the artery proximal to the fistula is occluded, have proved a valuable means of distinguishing between the two conditions.

CAUSATION

The causes of aneurysm are numerous but they may be classified rather broadly as inflammation, arteriosclerosis, trauma, embolism, or congenital defect. In the present series of aneurysms, external trauma accounted for 12 cases. One aneurysm of the brachial artery, one of the ulnar artery, and two of the popliteal artery were encountered in 4 patients who did not have any other evidence of inflammatory or degenerative disease of the arteries. Three patients who had popliteal aneurysms and one who had a femoral aneurysm were elderly and had obviously advanced arteriosclerosis. Two patients, each with several aneurysms, had extensive arteritis; in one, the diagnosis was clearly thromboangiitis obliterans, and in the other there was extensive migratory phlebitis associated with the arteritis. Three patients had syphilis and in each the aneurysm involved the popliteal artery.

Three patients had an aneurysm of the artery which supplied an arteriovenous fistula and the cause of the aneurysm seemed clearly to be the arterial degeneration caused by the arteriovenous fistula. One of us (Pemberton, 17), in 1930, suggested that the association of an aneurysm with an arteriovenous fistula should not be unusual because of the marked dilatation of the artery proximal to the fistula. As a result of this dilatation, there occur in the wall of the artery degenerative changes, probably produced by partial obstruction of the vasa vasorum. In this way, conditions become ideal for the production of the aneurysm. In one case in which there was a congenital arteriovenous aneurysm of the left foot an aneurysm of the left popliteal artery developed. In another case in which there was a congenital arteriovenous fistula of the right hand and forearm an aneurysm of the right brachial artery developed. In the third there were traumatic arteriovenous fistula involving the left superficial femoral vessels and a huge aneurysm of one of the retroperitoneal vessels in the pelvis.

The great majority of acquired arteriovenous fistulas are due to external trauma in which the vein and the artery are injured simultaneously. In the present series, 32 of the fistulas were caused by gunshot wounds and 6 by stab wounds. In 2 cases the fistulas were the result of a rupture of a spontaneous arterial aneurysm into a vein.

TREATMENT

There is some difference of opinion as to when traumatic arterial aneurysms should be operated on. The proponents of immediate operation hold that reparative and restorative operations may be employed more frequently

than is usual and that the dangers of pressure from a progressing hematoma will be lessened. On the other hand, the difficulties of operation in the presence of a hematoma and on a patient who has possibly recovered recently from shock are manifest, and, should repair of the injured artery be impossible, there is no alternative except ligation. There is also danger of infection since the operation is conducted in an infected field. Makins stated that operation should be postponed if the hematoma was of a duration of 3 days or more unless hemorrhage was continuing as shown by arterial leakage of blood, increasing tumor or increasing effects of pressure, or unless signs of extending infection were present.

In the present series, most of the traumatic arterial aneurysms were encountered here long after the stage of hematoma had passed. Operation was performed on two patients 1 month and 2 months respectively after they had sustained gunshot wounds of the popliteal artery and in each case it was necessary to ligate the popliteal artery. Both patients were young men and the results were satisfactory. Another patient who had a stab wound of the brachial artery sustained 2 weeks before he was seen here was treated expectantly with the hope that a more adequate collateral circulation would develop. Operation was made imperative, however, by a sudden increase of the size of the tumor. The artery was ligated above and below the site of injury and the vein was also ligated. The collateral circulation proved adequate.

There is general agreement (5, 16, 22) that corrective operations on acquired arteriovenous fistulas should be postponed for 3 to 6 months from the time of the injury to allow an adequate collateral circulation to develop. This delay, in addition, provides time for the absorption of the hematoma, for the subsidence of any infection that may have resulted from the injury and for the possible spontaneous cure of the fistula. In the present series, 3 patients were operated on within 1 month of the time of the injury. In one case, early operation was advised because of marked edema and persisting throbbing pain following a gunshot wound of the left popliteal artery. In another case, the mass about a brachial arteriovenous fistula enlarged progressively and it was thought that there was danger of a rupture of the sac. The third case was that of a gunshot wound of the shoulder that failed to heal and operation was undertaken under the erroneous clinical impression that the lesion was an infected gunshot wound. In each case the result after operation was satisfactory.

Collateral circulation. Before any operation that might involve ligation of the principal artery of an extremity is undertaken, the status of the collateral circulation should be estimated by the use of the Moszkowicz-Matas hyperemic test or one of its modifications (12), provided that the proposed site of the arterial obstruction is in a part of the body where the artery is accessible to compression. Should the collateral circulation be found to be inadequate, a program of systematic intermittent compression of the artery, according to the method of Matas, should be instituted. One of us (Pemberton) and McCaughan wrote in 1932 that when such preliminary tests gave evidence of efficient collateral circulation serious ischemia has never been observed in our experience to ensue after permanent occlusion of the artery. As a rule, since an arteriovenous fistula probably is the strongest of all stimuli for the production of collateral circulation, there need be little concern about the collateral circulation if the operation has been delayed for 3 to 6 months.

Such is definitely not the case with arterial aneurysms. Most often, in cases in which spontaneous peripheral arterial aneurysms develop the patients are old rather than young and the collateral vessels are likely to be the seat of some degree of arteriosclerosis. The aneurysm itself, as was pointed out by Theis, absorbs part of the force which normally is expended to drive the blood into the periphery. It is in such cases, in which the aneurysm involves the principal artery of the extremity, that the collateral circulation is often found to be doubtful or inadequate. In addition, it has been found from collected experience that the ligation of certain arteries, notably the popliteal, is followed by a high incidence of gangrene.

Lumbar sympathectomy has been proposed as a method both to increase the collateral

circulation and to prevent immediate postoperative vasospasm. Mulvihill and Harvey demonstrated, in dogs, that ligation of one or both external iliac arteries was always followed by a decrease of the temperature of the corresponding foot amounting to 10 to 30 degrees F. In most cases the temperature rose to the original level in about 13 hours. They found that the temperature of the extremity, which had fallen to that of the environment after the ligation of the artery, rose quickly to normal after the removal of the lumbar sympathetic ganglia and that the simultaneous removal of the ganglia with the ligation of the artery prevented the lowering of the temperature of the limb.

One of us (Pemberton) has performed endoaneurysmorrhaphy on 2 patients suffering from popliteal aneurysm on each of whom lumbar sympathectomy had been done previously as a specific measure to increase the collateral circulation. In each case the collateral circulation, as judged by the usual tests, including studies of cutaneous temperature, was doubtful. The results in each case were so striking that the records of the cases are worthy of review.

CASE 1. A white, American farmer, aged 58 years, was referred to the clinic in January, 1941, for treatment of a popliteal aneurysm, which had been present for 1½ years. About 6 months after the appearance of the tumor, there developed in the region an aching, intermittent pain which always disappeared after 1 or 2 days. There was no increase of the patient's symptoms until 3 weeks before he was seen here when the right leg became moderately swollen. Ten days later there developed in the right calf a severe cramp which lasted for 10 hours and the right foot became pale during this time. The next day another severe cramp set in but there was no change of the color of the foot. The calf remained tender following this attack and the leg became flexed at the knee so that the patient walked with difficulty.

On physical examination it was noted that the patient held the right leg flexed about 30 degrees at the knee. The blood pressure measured 160 millimeters of mercury systolic and 66 diastolic. There was a large pulsating aneurysm of the right popliteal artery, which measured 11 by 10 by 9 centimeters. The pulsations of the dorsalis pedis and posterior tibial arteries were absent on the right. On the left side the pulsations of these vessels were normal. Occlusion of the artery above the aneurysm produced marked pallor of the foot and there was no reactive hyperemia after the clamp was removed. There were slight venous engorgement and moderate edema of the leg. The results of urinalysis, the blood count and a roentgenogram of the chest were essentially normal. A flocculation test for syphilis gave negative results.

There was considerable doubt as to the adequacy of the collateral circulation; and, consequently, the patient was transferred to the Section of Neurologic Surgery and on January 29, 1941, extensive resection of the right splanchnic nerves with a portion of the right celiac ganglion and lumbar sympathetic trunk, including the 1st, 2d, 3d, and 4th sympathetic ganglia, was performed. Following the sympathectomy, the skin temperature of the right great toe was 33.5 degrees C. and that of the left great toe was 25.4 degrees C. (temperature of the air 25.5 degrees C.). In a cool room (air temperature 21.4 degrees C.) the temperature of the skin of the right great toe was 32.7 degrees C.; that of the left 22.1 degrees C.

Fifteen days after sympathectomy, endoaneurysmorrhaphy was performed. There was a perforating fusiform aneurysm of the right popliteal artery, which measured 8 to 10 centimeters in diameter. The popliteal artery was ligated proximally and distally with silk, the sac was opened and the blood clot was evacuated. The sac was then obliterated, surgical gut sutures being used. Following operation, the foot on the side on which operation had been performed was warmer than that on the other side. The patient made an uneventful recovery, and 3 months after the endoaneurysmorrhaphy, the right foot was still warmer than the left and the patient had been relieved of all symptoms.

CASE 2. The second patient was a Puerto Rican sugar plantation owner, aged 68 years, who had always been in good health until 10 months before coming to the clinic. At that time he had a cramping pain in the calf of the left leg for about 15 minutes. This pain had recurred periodically since, not always with exercise, but absolute rest always gave relief. The pain had persisted at times for several days. About 6 weeks before the patient was seen here, his left great toe became swollen, tender and cyanotic, and since then the entire left foot had been colder than the right and somewhat blue. The diagnosis of popliteal aneurysm was made elsewhere at the time when gangrene of the foot seemed imminent.

The pertinent findings on physical examination were as follows: The blood pressure measured 120 millimeters of mercury systolic and 70 diastolic. There was an aneurysm approximately 6 by 5 by 4 centimeters involving the left popliteal artery. The pulsations of the left dorsalis pedis and posterior tibial arteries were absent while pulsations were present in these vessels on the right. There was marked pallor on elevation of the leg with less marked rubor on dependency and clinical tests were interpreted as indicating a doubtful collateral circulation. All collateral pulsations disappeared when the aneurysm was compressed and there was marked pallor on elevation with persistent pallor on dependency. In addition to the findings in the leg,

evidence of bronchiectasis, an inguinal hernia and a moderately hypertrophied prostate were found. The temperature of the skin of the right great toe was 28.2 degrees C. and that of the left 27.8 degrees C. (air temperature 31.0° C.). With the aneurysm occluded by means of a clamp, the temperature of the skin of the right great toe was 32.5 degrees C. and that of the left great toe was 30 degrees C. (air temperature 31.0° C.; the patient had been in a warm room longer than when previous observations were made). The results of urinalysis, the blood count, and a roentgenogram of the chest were essentially normal. A flocculation test for syphilis gave negative results.

Left lumbar sympathetic ganglionectomy and trunk resection, including the 1st, 2d and 3d lumbar ganglia and intervening sympathetic trunk, were performed on August 11, 1942 by members of the Section on Neurologic Surgery. The day after sympathectomy the skin temperature of the right great toe was 27.1 degrees C. and that of the left was 32.3 degrees C. (observations made in patient's room; air temperature not recorded). Intermittent clamping of the artery proximal to the aneurysm was continued until it was possible to leave the clamp on for 20 to 30 minutes without the patient's suffering any particular pain.

Twenty days after sympathectomy, endoaneurysmorrhaphy was performed. It was found that practically the entire popliteal artery was involved by the aneurysm, which was 5 or 6 centimeters in diameter. The popliteal artery was ligated just proximal and distal to the aneurysm, the sac was opened and the clot was removed. The sac was then obliterated, surgical gut sutures being used. The day after operation the foot was of good color and the temperature of the skin of the two feet was practically the same. Five days later the temperature of the skin of the left great toe was 28.6 degrees C. and that of the right 27.0 degrees C. (air temperature 28.0° C.). The patient made an uneventful recovery and the left foot and leg remained warmer than the right.

ARTERIAL ANEURYSM

The following methods were used in the treatment of patients who had arterial aneurysms on the present series: (1) obliterative endoaneurysmorrhaphy with or without proximal and distal ligation, fourteen times; (2) proximal and distal ligation of the artery and excision of the aneurysm, twelve times; (3) restorative endoaneurysmorrhaphy, two times; (4) proximal ligation, two times; (5) a clamp was placed on the artery proximal to an aneurysm in 1 case, and the rupture elsewhere of an aneurysm that developed proximal to a congenital arteriovenous fistula led to amputation of the leg which was done elsewhere.

Obliterative endoaneurysmorrhaphy. This procedure, occasionally with the slight modification of extrasaccular proximal and distal ligation of the artery, or of proximal ligation of the artery, was employed more frequently than any other in the present series. As a rule, temporary compression of the main afferent and efferent arteries was effected while the sac was opened and the blood clot was evacuated. The status of the collateral circulation was evaluated further by releasing the temporary ligature on the efferent artery and noting the amount of retrograde bleeding (Henle-Coenen test, 18). The endoaneurysmorrhaphy was carried out, and permanent ties were substituted often for the tapes used to occlude the main arteries temporarily. The results after this operation were uniformly satisfactory, and in no case was gangrene observed. One patient who had popliteal aneurysm had edema of the leg after operation. One patient who had an aneurysm of the brachial artery, which had developed secondarily to a congenital arteriovenous fistula of the forearm, had so much pain in the region of the congenital fistula that amputation of the arm became necessary. There was no evidence of arterial insufficiency either clinically or from dissection of the surgical specimen.

Proximal and distal ligation of the artery and excision of the aneurysm. This procedure has the obvious advantage that there is no mass of tissue left behind at the site of the aneurysm, but it is more difficult technically than obliterative endoaneurysmorrhaphy, and there is greater interference with the surrounding structures and with the collateral circulation. It usually is the procedure of choice to treat aneurysms that involve secondary arteries of an extremity. In the present series, it was not limited to the treatment of such aneurysms but was performed in 4 cases of popliteal and 2 of superficial femoral aneurysm. The results were entirely satisfactory in 11 of the 12 cases. In the remaining case, an aneurysm of the superficial femoral artery, gangrene ensued in spite of the fact that the vein was ligated. This patient was 68 years of age and had marked peripheral arteriosclerosis.

Restorative endoaneurysmorrhaphy. This procedure was attempted in 2 cases only, both

TABLE I.—PERIPHERAL ARTERIAL ANEURYSMS IN SERIES. VESSEL INVOLVED, TYPE OF OPERATION AND RESULT OF TREATMENT

Artery involved*	Operative method	Results and comment
Popliteal	Obliterative endoaneurysmorrhaphy, 7 cases	All satisfactory. Edema of leg, 1 case. Two patients had previous lumbar sympathectomy
	Ligation and excision, 4 cases	All satisfactory
	Restorative endoaneurysmorrhaphy, 1 case	Satisfactory
	Amputation (elsewhere) 1 case	Aneurysm developed in artery leading to congenital arteriovenous fistula. Rupture of aneurysm led to amputation elsewhere
Femoral	Neff clamp, 1 case	No follow-up
	Obliterative endoaneurysmorrhaphy, 1 case	Satisfactory
	Proximal ligation Ligation and excision Excision entire femoral artery (elsewhere) } same case	Patient had had previous amputation. Large aneurysm in stump. After proximal ligation, aneurysm did not pulsate, but sac acted as foreign body. Necessary ultimately to remove entire femoral artery which was done elsewhere
Superficial femoral	Ligation and excision—vein ligated, 2 cases	Gangrene and amputation in 1 case
	Obliterative endoaneurysmorrhaphy, 3 cases	All satisfactory
	Restorative endoaneurysmorrhaphy, 1 case	Result poor. Patient stated he was not helped. Tumor present
Brachial	Obliterative endoaneurysmorrhaphy, 2 cases	In 1 case aneurysm in artery leading to congenital arteriovenous fistula. Amputation necessary because of pain
	Ligation and excision, 2 cases	Satisfactory results
Radial	Ligation and excision, 1 case	Satisfactory result
	Ligation, 1 case	Hematoma stage. Result satisfactory
Ulnar	Ligation and excision, 1 case	Satisfactory result
	Obliterative endoaneurysmorrhaphy, 1 case	Satisfactory result
Superficial volar arch	Ligation and excision, 1 case	Satisfactory result

*In some cases a patient had aneurysms of more than one artery.

operations having been done in the earlier years covered by the study. The result of the operation on a popliteal aneurysm was satisfactory. In the other case, in which there was a sacculated aneurysm of the superficial femoral artery, the operation seemed satisfactory technically, and the closure of the communication between sac and artery was reinforced by flaps taken from the sac. However, 10 months after operation, the patient still had a tumor and stated that his leg had not been helped in any way.

The other procedures listed have been used only in isolated instances and to cope with unusual situations.

In Table I the cases of arterial aneurysm are distributed according to artery involved, type of operation, and result of treatment.

ARTERIOVENOUS FISTULA

The following types of operation were used to treat the 40 patients who had arteriovenous fistula reviewed in the present series: (1) proximal and distal ligation of the principal artery and vein and excision of a segment of artery and vein with the communication (quadruple ligation and excision), sixteen times; (2) ligation of the communication between artery and vein, five times; (3) proximal ligation of the artery and vein, five times; (4) proximal ligation of the artery and vein and ligation or obliteration of the communication, five times; (5) other procedures.

Quadruple ligation and excision. Most authors agree that this is the procedure of choice for the radical cure of arteriovenous fistula, and our experience is in keeping with this view. Sixteen patients in the present series were treated in this manner with results that were entirely satisfactory for 14. It is evident that this procedure offers the best chance to cure the lesion and it was employed twice in the present series after the failure of other less radical operations. The only complication attributable directly to the operation was the death of one patient from a massive pulmo-

TABLE II.—ARTERIOVENOUS FISTULAS IN SERIES. ARTERY INVOLVED, TYPE OF OPERATION AND RESULT OF TREATMENT

Artery involved	Operative method	Results and comment
Femoral (In several cases external iliac actually ligated)	Quadruple ligation and excision, 3 cases	Results satisfactory
	Quadruple ligation and excision (common, profunda and superficial femoral ligated), 2 cases	Results satisfactory
	Proximal and distal ligation of artery (common, profunda and superficial femoral ligated). Vein not ligated, 1 case	Gangrene and amputation. Vessel in stump ruptured elsewhere 10 weeks later. Iliac ligated. Death elsewhere
	Proximal ligation artery and vein, 1 case	Massive arterial thrombus 5th day after operation. Gangrene and amputation
	Communication ligated, 2 cases	1 case recurrence, 1 case good result
	Proximal and distal ligation artery. Communication closed from inside artery, 1 case	Result satisfactory
Superficial femoral	Quadruple ligation and excision, 7 cases	1 case secondary aneurysm in pelvis, 1 case sudden death (pulmonary embolism) 5 hours after operation. Results satisfactory otherwise
	Quadruple ligation and obliteration or ligation of fistula, 2 cases	1 case recurrence of arteriovenous fistula. Cure followed quadruple ligation and excision. Result in other case good
	Quadruple ligation, 1 case	Still in hematoma stage—cure resulted
	Communication ligated, 1 case	Fistula recurred. No disability or progression of symptoms and nothing further advised
	Quadruple ligation and endoaneurysmorrhaphy, 1 case	Result satisfactory
Popliteal	Communication ligated, 2 cases	1 case result satisfactory. 1 case necessary to excise communication and to ligate vessels because of hemorrhage; gangrene and amputation followed
	Proximal and distal ligation artery and vein. Partial excision of sac, 1 case	Result satisfactory
	Proximal ligation artery and vein, ligation of communication, 1 case	Result satisfactory
	Restorative endoaneurysmorrhaphy, vein ligated, 1 case	Recurrence. No further treatment. Had thrill, ulcers
	Proximal and distal ligation of artery. Vein repaired, 1 case	Slight edema, otherwise satisfactory
Profunda femoris	Quadruple ligation, communication ligated, 1 case	Result satisfactory
	Proximal ligation artery and vein, 1 case	Thrill still present after operation. Ultimate cure from quadruple ligation and excision
Posterior tibial	Quadruple ligation and excision, 1 case	Result satisfactory
Peroneal	Proximal and distal ligation and excision of veins, 1 case	Result satisfactory
Subclavian	Fistula and vein ligated, 1 case	Good result
	Quadruple ligation and excision, 1 case	Good result
Axillary	Artery ligated above and below	Brachial plexus injury, operation 6 months later. Arteriovenous communication still open
	Vein ligated above, 1 case	
	Size of fistula reduced, 1 case	Chief injury to brachial plexus. Fistula still present
	Proximal and distal ligation, 1 case	In hematoma stage. Result satisfactory
Brachial	Quadruple ligation and excision, 2 cases	Results satisfactory
Digital	Amputation of finger, 1 case	Cure

nary embolism 5 hours after the conclusion of the operation. The patient had severe congestive heart failure due to an arteriovenous fistula involving the superficial femoral vessels.

Another patient who had an arteriovenous fistula of the superficial femoral vessels had, in addition, a huge aneurysm of one of the pelvic vessels. This was opened and packed. The circulation in the leg was adequate for 8 years but ultimately evidence of arterial insufficiency and venous stasis developed and the leg was amputated 14 years after the operation on the fistula.

Ligation or occlusion of the communication between the artery and vein. Practically, conditions for the employment of this procedure are encountered rarely, and there is always some

chance that the fistula may re-establish itself or that bleeding may develop because of degenerative changes in the walls of the fistula or in the vessels. It was attempted in 5 cases only and in 3 the results were unsatisfactory. In 1 case, serious bleeding necessitated reoperation, at which time the vein was ligated and a repair of the artery was attempted. This procedure was followed by gangrene, and amputation later became necessary. In another case, the thrill and bruit recurred on the 7th day after ligation of the fistula. This patient was cured ultimately by quadruple ligation and excision. The symptoms of the third patient who had recurrence did not progress and further treatment was not necessary.

Proximal ligation of artery and vein. This procedure was carried out in 5 cases with satisfactory results in 3. One patient had a recurrence within 1 year and in the other case there developed, on the 5th day after the femoral artery and vein had been ligated, a massive arterial thrombus which ultimately resulted in gangrene and amputation.

Proximal and distal ligation of artery and vein with ligation or occlusion of the communication. The results after this procedure were satisfactory in 4 of the 5 cases in which it was attempted. In 1 case a recurrence developed 18 months after the original operation. The patient was cured ultimately by quadruple ligation and excision.

In several cases in which the condition was treated before 1917, when Makins' work became known, the artery was occluded and the patency of the vein was maintained. In the light of present knowledge, such methods are largely obsolescent. Of the 5 patients treated by proximal and distal ligation of the artery and occlusion of the fistula, with repair of the vein, there were 2 cures, 1 case of gangrene, 1 case of chronic edema and ulceration, and 1 recurrence.

The vein and the communication between artery and vein were obliterated and the patency of the artery was maintained in 4 cases. Recurrence of the fistula occurred in 2 cases.

Other procedures, largely governed by the anatomic situation of the fistula, were used occasionally. An arteriovenous fistula situated in the finger was cured by amputation of the finger. In 2 cases of fistula involving the axillary vessels in both of which there was extensive injury of the brachial plexus, the condition was treated, in the 1 case by narrowing the fistula and in the other by proximal and distal ligation of the artery. The procedures in both cases were limited because of the danger of further injury of a nerve. Another patient, who had an axillary arteriovenous fistula still in the hematoma stage, was operated on under the erroneous impression that the lesion was an infected wound. A cure resulted from proximal and distal ligation of the artery.

In Table II the cases of arteriovenous fistula are distributed according to the artery involved, the type of operation performed, and the result of treatment.

SUMMARY

From a review of the records of 67 patients who suffered from acquired, peripheral aneurysm and arteriovenous fistula and who were treated by operation at the clinic, it would seem that the exact diagnosis can be made usually before operation and that a correct evaluation of the status of the collateral circulation is possible by means of clinical tests before operation and by noting the amount of retrograde bleeding from the principal artery at the time of operation (Henle-Coenen test). In cases of arterial aneurysm of the leg in which there is doubtful collateral circulation, much improvement can be expected to follow lumbar sympathectomy, and postoperative vasospasm is also prevented. Endoaneurysmorrhaphy with or without extrasaccular ligation of the principal artery, and proximal and distal ligation of the artery and excision of the sac are the procedures of choice for the treatment of aneurysms of peripheral arteries. In the case of peripheral arteriovenous fistula, the procedure of choice for the radical cure of the condition is clearly quadruple ligation and excision. Another satisfactory but less certain procedure is quadruple ligation and obliteration and occasionally simple ligation of the communication between artery and vein may be carried out.

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A NEW TEST FOR PANCREATIC FUNCTION

II. Experimental Observations

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THE results of animal experiments concerning a new pancreatic function test, applicable to use in the human, were published recently (3). The diagnostic possibilities of changes in blood amylase or lipase following vigorous stimulation of the external pancreatic secretion with either mecholyl (acetyl-β-methylcholine chloride)[1] plus eserine or with secretin were demonstrated. The minimal doses of mecholyl and eserine, which would cause an increase of the two blood enzymes in cases with a normal pancreas, were established, and it was shown that these doses could be further reduced by giving the drugs twice at a 15 minute interval. Several weeks after obstruction of one or both pancreatic ducts, when atrophy of the glandular tissue had occurred, no increase of blood enzymes occurred following the administration of the drugs mentioned. It seemed probable that in clinical cases the injection of mecholyl and eserine would enable us to uncover pathological processes of the pancreas, characterized by decreased production of pancreatic juice, such as atrophy of the pancreas, chronic pancreatitis, cirrhosis of the pancreas, or secretory insufficiency. The doses of mecholyl and eserine used in these experiments, though causing no untoward reactions in dogs, were still too great to be applied safely to the human. Smaller doses, however, may prove effective for clinical use.

In a second series of experiments secretin was used. The maximum dose of this drug was determined, which did not cause an increase of blood enzymes in the presence of a normal pancreas. In animals with obstructed pancreatic ducts, injection of this dose of secretin was followed almost regularly for several weeks after operation by an increase of the two blood enzymes, especially of the blood lipase. Applied to the human this procedure can be expected to reveal disturbances to the normal flow of the pancreatic juice, as may occur in tumors of the pancreas or of the papilla, pancreatic cysts, pancreatic stones and, possibly, subacute pancreatitis.

Comfort and Osterberg in studies on the human have shown that the combination of mecholyl and secretin stimulated pancreatic secretion more vigorously than any other drug or combination of drugs tried. Although their procedure of duodenal aspiration and of enzyme determinations in the duodenal contents was different from our procedure of employing changes in serum enzymes for the determination of pancreatic function, it was apparent that their method of stimulation of the pancreas by mecholyl plus secretin might be useful for our test.

METHODS

The effects on blood lipase of varying doses of mecholyl plus secretin were assayed on normal dogs first and, after an adequate dosage had been established, on dogs with obstructed pancreatic ducts. Obstruction was produced by ligation and division of one or both pancreatic ducts, with or without partial separation of the pancreas from the duodenum. All animals were reoperated upon at appropriate intervals in order to ascertain the condition of the pancreas; biopsies of the pancreas were taken for histological study.

The animals were starved for 20 hours before the experiments. A control sample of venous blood was drawn first, and then mecholyl was injected subcutaneously. Five minutes later, secretin in a 100 milligrams per cent solution was slowly injected intravenously. Blood samples were drawn 30, 60 and 90, or 120 minutes after the injection of mecholyl. Serum lipase determinations by the method of Crandall and Cherry were performed im-

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[1] Mecholyl, supplied by Merck and Co.

TABLE I.—THE EFFECTS OF MECHOLYL AND OF SECRETIN ON THE SERUM LIPASE OF NORMAL DOGS

No. of dog		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Mecholyl mgm. per kgm., subcutaneously		0.111	0.133	0.15	0.154	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.244	0.275
Secretin mgm. per kgm., intravenously		3	3	2	2	3	3	2.5	2.5	2	2	2	2	2	2	3	3
Serum lipase after minutes	0	0.6	1.0	0.3	1.2	0.8	0.4	0.2	0.4	0.2	1.8	0.4	0.4	0.2	0.5	0.4	0.2
	30	0.4	1.0	4.1	2.1	1.2	1.2	2.2	1.7	4.2	2.4	1.3	1.2	3.0	1.3	2.3	2.9
	60	0.4	0.6	4.1	1.6	1.8	1.0	2.0	1.8	4.0	2.8	1.2	0.9	2.6	1.2	2.3	4.0
	90	0.4	1.0	3.9	1.9			1.8	1.6	4.0	3.0	1.0	0.7	2.6	1.0		
	120															2.0	4.0

mediately after the termination of the experiment. The values for serum lipase in Tables I to III are expressed as cubic centimeters of a twentieth normal solution of sodium hydroxide per cubic centimeter of serum. Serum amylase was not determined because previous experience with secretin (3) had shown that the values of the serum lipase gave more reliable information than those of the serum amylase.

RESULTS

Sixteen normal dogs received injections of 0.111 to 0.275 milligram of mecholyl and of 2 to 3 milligrams of secretin per kilogram of body weight. Previous experiments with secretin alone (3) had shown that this dosage usually did not cause an increase of serum lipase in normal dogs.

Dogs 1 and 2, which received 0.111 and 0.133 milligram, respectively, of mecholyl and 3 milligrams of secretin per kilogram of body weight, showed no change of serum lipase exceeding the range of normal fluctuations (Table I). All dogs receiving 0.15 to 0.275 milligram of mecholyl and 2 to 3 millograms of secretin per kilogram (Nos. 3 to 16), showed

TABLE II.—THE EFFECTS OF MECHOLYL AND OF SECRETIN ON THE SERUM LIPASE OF DOGS WITH OBSTRUCTED PANCREATIC DUCTS

Dog No.	Minutes after injection	Days after obstruction														
		0	16	17	23	27	30	55	57	59	63	76	84	105	113	240
1	0			0.5						1.4			1.1		1.0	
	30			0.4						5.7			1.1		1.2	
	60			1.5						4.1			1.2		0.7	
	90			1.4											0.7	
5	0	0.8					1.4			2.2		1.3		0.8		
	30	1.2					5.7			5.2		1.3		1.0		
	60	1.8					4.1			4.8		1.1		0.8		
	90									4.4		1.5		0.6		
9	0	0.2			0.4											
	30	4.2			3.2											
	60	4.0			2.6											
	90	4.0			Died											
10	0	1.8					1.0		0.8				0.5			
	30	2.4					1.6		2.0				0.2			
	60	2.8					1.6		2.0				0.4			
	90	3.0					1.2		1.8				0.2			
11	0	0.4	1.2				1.5				0.6					
	30	1.3	2.0				1.7				0.7					
	60	1.2	1.5				1.6				0.8					
	90	1.0	1.3				1.6				0.9					
13	0	0.2	0.6					0.7								
	30	3.0	1.2					0.9								
	60	2.6	0.4					1.0								
	90	2.6						0.9								
17	0															0.3
	30															0.4
	60															0.4
	90															0.4

TABLE III.—PERSISTENT POSITIVE LIPASE TESTS FOLLOWING OBSTRUCTION OF THE PANCREATIC DUCTS OF DOGS

Dog No.	Minutes after injection	Days after obstruction										
		0	16	30	38	44	59	67	76	84	105	106
4	0	1.2		1.5			1.6		1.2		1.9	
	30	2.1		3.3			4.6		4.3		3.1	
	60	1.6		2.7			4.2		3.8		2.6	
	90	1.9					3.6		3.5		2.7	
14	0	0.5	0.4			1.0				0.4		
	30	1.3	2.8			3.2				1.0		
	60	1.2	2.2			2.1				0.7		
	90	1.0				2.5				0.7		
18	0				0.9			1.2				0.3
	30				2.8							4.5
	60				3.0			2.4				3.1
	90							2.0				1.1

a marked increase of serum lipase, with a peak 30 to 60 minutes after the injection. No untoward reactions were observed. We, therefore, decided to use a standard dosage of 0.22 milligram of mecholyl and of 2 milligrams of secretin per kilogram because in our experiments its effectiveness was always distinct and reliable, and because the dosage of mecholyl was below the maximal subcutaneous dose which can be used in the human.

After having established a dosage of mecholyl and of secretin which caused a consistent increase of serum lipase in normal dogs, we proceeded to experiment on 10 dogs with obstructed pancreas. In 7 of these animals, a mecholyl-secretin test had been performed prior to the obstruction (0.015 mgm. mecholyl per kgm. in one animal and 0.022 mgm. in the other animals).

Dogs 1, 5, 9, 10, 11, and 13 had a positive serum lipase response to the injections up to 16 to 59 days after operation. When the tests were repeated 30 to 84 days, respectively, after operation, they were negative. Likewise in dog 17, 240 days after operation, the test was negative (Table II).

Three dogs had a persistently positive lipase reaction 84, 105, and 106, days, respectively, after the operation (Table III). At reoperation it was found that in none of them atrophy of the pancreas had occurred, but that only a moderate degree of induration was present. On the other hand, 6 of the 7 dogs with a negative test 30 to 84 days after obstruction (Table II) showed an advanced degree of cirrhosis and atrophy of the pancreas, such as is usually seen some time after complete obstruction. However, the 7th dog (No. 5) with negative lipase reactions 76 and 105 days after obstruction, had an almost normal pancreas. We were not able to find an explanation for this latter finding.

ANALYSIS OF STUDY

Our results show that in normal dogs injection of mecholyl plus secretin in the aforementioned doses regularly caused a marked increase of serum lipase, which reached its peak usually 30 to 60 minutes after injection. Following obstruction of the pancreas, in some dogs, the lipase response was greater than before for several weeks (Nos. 4, 5, 13, 14) while in other dogs it remained almost the same (Nos. 9 to 11). This demonstrated, that the mecholyl plus secretin test was not useful in *acute* obstruction of the pancreas. If the obstruction was not followed by cirrhosis and atrophy of the pancreas, the test, with one exception, remained permanently positive. If, however, a permanent damage to the glandular tissue of the pancreas ensued, the mecholyl-secretin test became consistently negative.

These results justify the conclusion that determination of serum lipase after administration of mecholyl plus secretin gives significant information concerning the functional ability of the pancreatic gland and that it may be used successfully in humans for the diagnosis of disorders of the pancreas, as, for example, functional insufficiency, chronic pancreatitis, or pancreatic cirrhosis.

These mecholyl-secretin tests yielded results similar to those previously reported with

the combined administration of mecholyl and eserine (3), but they were more consistent, and they were obtained with doses of mecholyl which may be used in the human, while the previously reported doses of mecholyl and of eserine were too large for clinical application (3).

The previously reported administration of secretin alone did not cause an increase of serum enzymes in dogs with a normal pancreas, while after obstruction of the pancreas, secretin tests revealed a marked response of serum enzymes, which could be repeated for several weeks.

We have thus employed two types of stimulation of the pancreas for our diagnostic tests. For the first type of stimulation a dose of secretin was chosen which did not produce an increase of serum enzymes in the presence of a normal pancreas, but raised them in the case of pancreatic obstruction. The second type of stimulation was produced with a stronger stimulant, mecholyl plus secretin, which raised blood enzymes in the case of a normal pancreas as well as in the case of pancreatic obstruction but not in case of severely damaged glandular pancreatic tissue. In clinical use the latter, more severe, test would have to be employed only after the first and milder one would be negative. Both tests are not necessary in the very acute stages of pancreatitis in which stimulation of pancreatic secretion might be harmful and in which simple determination of serum amylase or lipase without stimulation will give sufficient information, by showing increased enzyme levels.

Two of the main features of pathology of the pancreas, obstruction to the outflow of pancreatic juice, and insufficient production of pancreatic juice, can be revealed by studying the serum lipase following administration of secretin alone and of mecholyl plus secretin.

SUMMARY

Stimulation of pancreatic secretion with mecholyl plus secretin caused an increase of serum lipase in normal dogs, while in the case of cirrhosis and atrophy of the pancreas no increase of serum lipase occurred.

The administration of mecholyl plus secretin may be used as a test for the secretory ability of the pancreas.

In clinical use the administration of secretin alone and of mecholyl plus secretin may supplement each other successfully in the diagnosis of obstruction and of secretory insufficiency of the pancreas.

Clinical tests with secretin and secretin plus mecholyl are in progress.

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STUDIES ON THE THERAPY OF HEMORRHAGIC SHOCK

II. The Effects of Iso-Osmotic and of Concentrated Serum and Plasma in Dehydrated Dogs

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IN a previous paper (11) the therapeutic effects of iso-osmotic and concentrated plasma protein solutions on hemorrhagic shock in normal dogs were compared. In this paper a comparable study on dehydrated dogs is presented.

The procedures were the same as previously described. Shock was produced by graded bleeding in unanesthetized dogs and iso-osmotic or concentrated canine serum or plasma was administered to animals at different levels of circulatory collapse. In the warmer weather the animals were deprived of both food and water for 18 to 30 hours before each experiment. In the colder weather this period of fluid deprivation was inadequate. It was necessary to place the animals on a dry diet and to restrict water intake for 48 to 72 hours. The individual variability of the animals and the complexity of the factors influencing the state of hydration made it difficult to estimate the degree of dehydration of the individual animal before the experiment. Unfortunately, the normal values for thiocyanate dilution vary markedly with size, age, sex, and other factors and, therefore, give no valid index of the degree of dehydration of the individual animal (5).

Because the degree of shock has an important bearing on the response to infusion, two comparable groups of animals in various degrees of shock were infused with iso-osmotic or with concentrated serum or plasma, and the clinical response, cardiovascular, and blood changes, and survival times were studied after infusion.

From the Samuel Deutsch Serum Center and from the Department of Gastro-Intestinal Research of Michael Reese Hospital, Chicago. V. Weissman was most helpful in the carrying out of this study.

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EXPERIMENTAL OBSERVATIONS

In an earlier publication the influence of dehydration on the development of posthemorrhagic shock has been discussed (15), with particular emphasis on the hemoconcentration which frequently follows hemorrhage in dehydrated animals. Due to the decreased fluid reserve resulting from water deprivation, dehydrated animals cannot compensate for blood loss as well as normal animals. Thus, dehydrated animals after less bleeding develop severer degrees of circulatory collapse or shock than do normally hydrated dogs. Many such animals either expire during or shortly after the completion of the 26 minute period required for the posthemorrhage plasma volume determination, or else deteriorate so badly that recovery after any type of infusion could not be expected.

This inability of the dehydrated animals to compensate for loss of blood was particularly notable in the summer months when, not infrequently, animals deprived of water for only 18 hours would develop severe shock after a single hemorrhage totalling only 25 to 30 per cent of the initial blood volume. In such an animal, the blood pressure, instead of gradually rising above the low level at the end of the bleeding period, would continue to fall and the animal's general condition one-half hour or so after the hemorrhage obviously would be critical. At this time, many of these animals would have an increased hematocrit and, subsequently, either would fail to live through the blood volume determination or would be beyond the point where they could be restored completely by infusion.

In the colder weather, animals deprived of water for only 18 hours reacted to hemorrhage in the same manner as did normal dogs, sometimes tolerating as many as four or five re-

peated hemorrhages with progressive hemodilution maintaining the plasma volume, blood pressure, and carbon dioxide at diminished, but above shock, levels. Moreover, in these animals the response to either concentrated or iso-osmotic infusions was similar to that observed in normal animals. For these reasons, the more extreme measures for achieving dehydration in the colder weather were employed. These differences in fluid reserve with seasonal changes in temperature are not difficult to understand, inasmuch as the dog's principal loss of fluid by evaporation occurs during panting and this is usually minimal in the colder weather.

TREATMENT OF POSTHEMORRHAGIC SHOCK IN DEHYDRATED DOGS WITH ISO-OSMOTIC SERUM OR PLASMA[1]

The clinical response immediately following infusion of iso-osmotic serum or plasma was good in all 9 dehydrated animals studied, but it was not as consistent or as striking as that observed in the normal animals (11). Although most of the dogs could stand when removed from the table, some were weak and made no effort to walk. Canine serum was used after mild to severe hypocalcemic tetany was encountered in all of the animals which received citrated plasma. In one experiment, a reaction of this nature probably contributed to the ultimate death of the animal. However, there was a marked improvement in the condition of nearly all of the animals as soon as the infusions were started. As in the normal group, animals which were pulseless and receiving artificial respiration exhibited a cardiovascular recovery and resumed spontaneous respiration within a few minutes of the start of the infusion.

The blood pressure in all of the dehydrated animals infused with iso-osmotic serum and plasma reached maximal levels which were well above shock levels within 10 to 15 minutes, but in none was the recovery as complete or as well maintained as in the normal animals infused with iso-osmotic solutions (11). After the withdrawal of the blood samples for the postinfusion plasma volume determination, the blood pressure in most of the dehydrated animals had dropped 10 to 20 millimeters mercury, indicating a greater susceptibility to blood loss after infusion than in the normal animals. Similarly, the general condition of some of the animals at the end of the experiment had deteriorated to a certain degree; as a matter of fact, a few of the animals which died during the night were unable to walk and had to be carried to their cages at the end of the day.

The improvement in clinical condition and blood pressure, in general, was accompanied by like changes in other experimental data. The circulating time improved in all animals after infusion. The plasma volume was increased considerably in every animal, but, in this respect, also, the restoration was not as marked as in the normal animals receiving iso-osmotic solutions (11) for in only 5 of the 9 dehydrated animals was the plasma volume after infusion significantly greater than the prehemorrhage plasma volume, despite the large volumes of fluid administered. The plasma protein concentration returned to within normal limits after infusion in nearly all animals, but the total circulating protein in those animals which had less satisfactory plasma volume recoveries did not rise above the prehemorrhage values, as it had in all of the normal animals which received iso-osmotic infusions.

Excluding the one animal (No. 12) which had a severe tetany and died during the night, the other 3 dehydrated animals with carbon dioxide levels above 15 volumes per cent, like the comparable normal animals (11), all survived more than 24 hours. On the other hand, of the dehydrated animals with carbon dioxide levels below 15 volumes per cent, 4 died during the night and 1 lived for 17 hours after the infusion. The carbon dioxide recovery after infusion was good in every animal of this group but 1 (No. 18). However, in some of these dehydrated animals the carbon dioxide was not of as great prognostic significance as in the normal group. For example, in animals Nos. 14 and 17; the recovery of blood pressure, circulating time, and carbon dioxide after infusion was apparently satisfactory; nevertheless, the animals were found dead in the morning.

[1] Complete tables will be found in the authors' reprints.

TREATMENT OF POSTHEMORRHAGIC SHOCK IN DEHYDRATED DOGS WITH CONCENTRATED SERUM OR PLASMA

The administration of concentrated citrated plasma (see animals Nos. 32, 34, and 38) to dehydrated dogs in shock led to such severe reactions, including sudden death probably from cardiac arrest due to the extreme hypocalcemia, that concentrated serum was used, subsequently. The apparent overburdening of the circulation observed following the administration of concentrated plasma protein solutions to normal dogs (11) frequently occurred in the dehydrated animals, as well. In at least one experiment (No. 31), this circulatory embarrassment possibly played a rôle in the death of the animal 45 minutes after the injection for the animal's carbon dioxide level was well above 15 volumes per cent and the expectancy of recovery was good.

As in the normal animals which received concentrated plasma protein solutions (11), the response of the dehydrated animals to concentrated material was slower and less marked than that observed following iso-osmotic infusions in either normal or dehydrated dogs. Even after the blood pressure had reached its maximal levels 15 to 30 minutes after the injection, nearly all of the animals were weak and unable to stand, and some were still comatose. By the time of the post-infusion plasma volume determination, the condition of the animals had improved somewhat, but, in every case, the small amounts of blood required for this determination led to a further deterioration in the animal's condition so that many of the animals were moribund when returned to the cages and died during the night.

The poorer response of the dehydrated animals to concentrated serum or plasma was also disclosed by the laboratory findings. The blood pressure recovery in all animals was delayed, and the maximal level attained was generally lower than that observed following iso-osmotic solutions in both normal and dehydrated dogs, although it was equivalent to that observed following concentrated solutions in normal dogs (11). Moreover, the fall in the blood pressure following the small amounts of blood withdrawn for the final plasma volume studies was much greater than that observed in any of the other groups.

The plasma volume recovery in the dehydrated dogs following concentrated plasma protein solutions was somewhat better than the clinical improvement and survival times would indicate. The postinfusion plasma volume in all the animals which survived long enough to permit the determination was equal to, or greater than, the initial (prehemorrhage) value in contrast to the normal animals which received four times concentrated solutions.

The arterial plasma carbon dioxide recovery in the dehydrated dogs receiving concentrated solutions was poor in comparison with that of the animals receiving iso-osmotic solutions and there was a better correlation between prognosis and carbon dioxide recovery than in the latter group. Again, the arterial plasma carbon dioxide level at the time of the infusion was important in evaluating survival.

Survival times of the dehydrated dogs receiving concentrated solutions at all levels of arterial plasma carbon dioxide content were poorer than those of the other groups (11). Only 1 of the animals with an arterial plasma carbon dioxide content of more than 15 volumes per cent lived for more than 24 hours, 3 survived the experimental day, and were found dead in the morning, 1 died during, and another shortly after, the injection of concentrated plasma, and 1 lived 45 minutes. Of the animals of this series with arterial plasma carbon dioxide levels below 15 volumes per cent before infusion, only 1 survived the experimental day, 1 died 5 minutes after the injection of concentrated plasma, and 4 survived 3 hours or less.

EVALUATION OF STUDY

The influence of dehydration on the genesis and therapy of shock has been mentioned by many reviewers but few experimental investigations of this problem have been reported. Blalock found that deprivation of food and water in unanesthetized dogs led to no change in the average total amount of blood which could be removed by graded bleeding before death. Calvin, on the other hand, observed that dehydrated dogs hemodiluted less than

did normal controls when subjected to severe single hemorrhages which did not produce circulatory collapse.

Our results indicate that the decrease in fluid reserves following water deprivation in dogs has a profound influence on the development and treatment of shock following multiple graded bleedings. The dehydrated animals not only developed a more severe shock after less bleeding but also did not respond as well to either iso-osmotic or concentrated serum or plasma than did the normal dogs (11). More important than this, however, these experiments demonstrate that in dehydrated and in normal animals concentrated plasma protein solutions are definitely inferior to iso-osmotic solutions in the treatment of posthemorrhagic shock. In all degrees of posthemorrhagic circulatory collapse, mild to severe, the clinical response, blood pressure, and carbon dioxide recovery, resistance to additional blood loss, and survival times of the dehydrated animals receiving concentrated serum or plasma was decidedly poorer than that of dehydrated or normal animals receiving iso-osmotic solutions or of normal animals receiving concentrated solutions (11).

In the last decade the factor of dehydration in the surgical patient has received a great deal of attention from experimental and clinical investigators alike. As a result, the water balance of the surgical patient today is carefully protected both before and after operation. However, this achievement of laboratory and clinical science has led some to regard the well hydrated condition of the hospitalized patient as the normal state and to forget that water balance in the surgical patient is not a simple matter which can be adjusted by the rapid administration of large volumes of fluid, at any time. If the patient is to be guarded against the consequences of fluid loss in insensible and visible perspiration, in feces and urine, in respiration, and in hemorrhage or exudation during the operation, preoperative fluid administration must be started early and continued after operation, particularly in patients who can take nothing by mouth. As great as are the fluid requirements of the normal patient, the requirements of the dehydrated patient obviously must be greater. Coller and Maddock, for example, suggest that at least 7 liters of fluid are needed to correct the fluid balance in a severely dehydrated patient, exclusive of the fluid lost through abnormal channels such as fistulas, internal hemorrhage, and such.

More recent experimental studies, moreover, have weakened the older concept that the extracellular or interstitial fluid constitutes a protective reservoir of freely moving fluid which must be depleted before any changes occur in the intracellular or the intravascular water. From the work of Hastings and of Peters and their associates there has evolved the concept of the body fluids and solids forming an iso-osmotic system in which semi-permeable membranes maintain the solid content of the three phases—intravascular, interstitial, and intracellular—with water transfer maintaining an equilibrium and a uniform osmotic pressure in all. Thus, simple dehydration due to water deprivation, experimentally should produce an eventual decrease in the total volume, and an increase in the concentration of solids in each of the 3 phases.

Hamilton and Schwartz found in dogs that simple water deprivation led to concentration of all body fluids. Mellors and associates (9, 10) reported that in dogs dehydrated by several methods the shifts of fluid were in accord with this concept and that early in dehydration of any type there occurred a decrease not only in the interstitial fluid volume but in the plasma volume as well. Elkinton and Taffel reported that in dogs, dehydrated by deprivation of food and water for long periods, progressive hypertonicity of all body fluids developed and a substantial loss of intracellular as well as interstitial fluid occurred, with an increased excretion of potassium in the urine. Furthermore, Stewart and Rourke have presented evidence that, following hemorrhage in normally hydrated animals, intracellular as well as extracellular fluid is drawn into the circulation. Consequently, in evaluating fluid exchanges, it is incorrect to regard 15 per cent of the body weight as freely available interstitial fluid which is readily mobilized to maintain the plasma volume, without any influence upon the intracellular fluid.

These considerations are important in any attempt to weigh the potential usefulness of a blood substitute, particularly in war time. The wounded soldier on the field of battle is not the well hydrated patient in the hospital. Under the stress of modern warfare with the widely varying climatic conditions and frequent dislocation of supplies, dehydration of the military or civilian casualty before injury is not uncommon. In addition, the injured may remain untreated in the field for some time, losing fluid and electrolytes in bleeding or exudation from the wound or in vomiting, with resultant oligemia and tissues severely depleted of fluid.

Second, it should be recognized that there are definite limitations to the amount of fluid which can be shifted to the vascular system without seriously affecting the osmotic relations of the interstitial and intracellular fluid, and that these "available" fluids are rapidly depleted by continued bleeding or by dehydration. Our experiments, in normal as well as in dehydrated dogs, demonstrate that concentrated plasma protein solutions, consequently, are not as effective as iso-osmotic plasma protein solutions in the treatment of posthemorrhagic shock, because water cannot be safely withdrawn from the tissues beyond certain limits.

In normal dogs with milder degrees of shock as represented by higher arterial plasma carbon dioxide levels before infusion, the decrease in blood volume and the depletion of the fluid reserves of the body are not too severe so that at times even saline solution will be sufficient to maintain life. In such animals, concentrated plasma protein solutions can sufficiently restore the blood volume without any serious consequences. However, the clinical response, as well as the resistance to further blood loss, is poor in these animals which, after the infusion of concentrated plasma protein solutions, are, in effect, dehydrated animals unless additional fluid is simultaneously or subsequently administered. In normal animals in severer degrees of shock or in dehydrated animals, even in lesser degrees of shock, the decrease in blood volume and in fluid reserves after graded bleeding is more profound so that saline infusions rarely give a favorable response. In these animals, concentrated plasma protein solutions, although tending to increase the plasma volume, lead to much poorer results than do iso-osmotic solutions, and this is reflected by all the experimental observations—recovery of blood pressure and carbon dioxide levels, clinical condition, survival times, etc. Apparently the increase in plasma volume and the temporary improvement in the circulation which occurs is achieved at the expense of not only interstitial but also of intracellular fluid, with added injury to tissues already damaged by the consequences of the impaired circulation.

The importance of the state of hydration in determining the effects of therapy in shock is illustrated further by the results with iso-osmotic plasma protein solutions in the dehydrated dogs. Apparently the already decreased extravascular fluid reserves in these animals were further depleted by the repeated hemorrhages, creating an extreme tissue dehydration which drew heavily upon the fluid later infused as iso-osmotic serum or plasma. Thus, the plasma volume recovery in these animals was not as good as in the normal animals which received similar infusions at comparable levels of shock, and the other laboratory findings, clinical response, and survival times reflect this discrepancy.

The differences between concentrated and iso-osmotic serum and plasma, in both normal and dehydrated dogs, were especially marked when comparable animals at severer degrees of shock are considered. In making this comparison, we have found that the response to the infusion had a definite relation to one important index of the animal's condition—the arterial plasma carbon dioxide content at the time of infusion—when the hemodynamic criteria of shock, hypotension, and decreased circulation time, were present. Thus, the clinical condition, or the blood pressure, or the circulating time of the animal at the time of infusion could be at "extreme shock levels" but if the carbon dioxide content were above 15 volumes per cent, the probability of the animal's surviving even with saline solutions would be better than if the carbon dioxide content were very low and the other criteria at less critical levels.

That the carbon dioxide content at the time of infusion should give a better index of the degree of shock and the response to infusion is not surprising for, unlike blood pressure, hematocrit, or circulating time, which give only an instantaneous picture of the condition of the circulation at a particular moment, the carbon dioxide content is a time intensity factor which measures not only how much, but also how long the circulation has been impaired. Riegal has demonstrated and we have confirmed (6) that, following hemorrhage, the progressive decrease in arterial carbon dioxide content results from the continued accumulation in the blood of lactic acid and other products of defective tissue metabolism due to tissue ischemia and anoxia. Thus, the carbon dioxide level to a certain extent is a measure of the degree of tissue damage in shock and, consequently, should be a good index of the response to therapy.

The use of the arterial plasma carbon dioxide content instead of the carbon dioxide combining power as an index of the alkali reserve may be questioned on the grounds that a transient hyperventilation may lead to a lowering of the arterial carbon dioxide content, which could be misinterpreted as indicating an increased acidosis. However, we have found that, even in unanesthetized dogs, the arterial plasma carbon dioxide content and the plasma carbon dioxide combining power drop almost proportionately as shock develops, the combining power, of course, always remaining somewhat higher than the content. Consequently, we have used only the arterial plasma carbon dioxide content, because the technical difficulties in the combining power determination make this procedure more time consuming and less accurate than the determination of the arterial plasma carbon dioxide content.

In the treatment of shock the primary consideration is the safety and effectiveness of the therapeutic agent. Ease and cost of preparation, facility of transport and storage, speed and ease of administration, are all to be considered—and particularly in relation to the widely varying conditions under which the present global war is being waged. However, the ultimate decision as to the use of a blood substitute must rest on its safety and effectiveness in the treatment of shock under all conditions encountered in the field. These studies demonstrate that concentrated plasma protein solutions are less effective in the treatment of posthemorrhagic shock in normal as well as in dehydrated animals. Therefore, although the use of concentrated solutions presents attractive possibilities and may be satisfactory under certain conditions, isoosmotic protein solutions appear preferable for routine use, and particularly when dehydration may be a factor.

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WOUND HEALING
EXPERIMENTAL AND STATISTICAL STUDY
V.—Bacteriology and Pathology in Relation to Suture Material

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RATS are very resistant to infection. Among the several hundred animals that were operated upon with the sterile technique previously outlined, only two gross wound infections were observed. However, since it has been shown (1) that practically all operative wounds are contaminated, usually by air-borne bacteria during the course of an operative procedure, it was thought advisable to determine what percentage of our wounds contained such bacteria. Cultures were performed for aerobic organisms only, since this study is not primarily one of the bacteriology of wounds.

Catgut. Twelve of the 60 cultures made (20 per cent) of the catgut sutured wounds showed positive cultures. The organisms encountered were: Staphylococcus aureus, nonhemolytic streptococcus, pyocyaneus, and colon bacillus.

Silk. Four of the 56 cultures made (7.1 per cent) showed positive cultures. Three of the wounds showed Staphylococcus aureus and 1 a nonhemolytic streptococcus.

Wire. Four positive cultures (7.8 per cent) were obtained from 51 cultures made, 2 of which showed Staphylococcus aureus and 2 nonhemolytic streptococcus.

Cotton. Cultures are available in only 43 of the 56 animals in this group. Two positive cultures (4.7 per cent) both containing nonhemolytic streptococcus were obtained.

Nylon. Four positive cultures of the 55 made, giving a percentage of 7.3 per cent of the total, were obtained. The organism in all cases was a Staphylococcus aureus.

Table XIX presents a summary of the results of the bacteriological study of wounds sutured with the various suture materials.

Organisms were cultured from 20 per cent of catgut wounds, and from 4.7 to 7.8 per cent of nonabsorbable sutured wounds. This marked difference in the incidence of positive cultures we believe is consequent to the more severe inflammatory reaction observed in the catgut wounds. In short, the catgut wounds presented a better medium for bacterial growth. Furthermore, these wounds, because of the marked degree of inflammation present, were not able to cope with bacteria as well as were the wounds sutured with nonabsorbable sutures. This may explain in part the greater percentage of wound infections observed clinically in catgut sutured wounds in comparison with silk sutured wounds (2). Meleney has stated that the most important factor in the reduction of wound infections observed at the Presbyterian Hospital was the change of suture material from catgut to silk.

PATHOLOGY

We shall not attempt to describe minutely the gross pathological changes in the wounds since a microscopic examination gives a more accurate appraisal.

HISTOPATHOLOGY

Catgut. Sections made on the 1st postoperative day show slight edema and only small amounts of fibrin. The sutures are intact and there are collections of polymorphonuclear cells about them. Collagen and fibroblasts are not noted and vascular changes are limited to dilatation of pre-existing capil-

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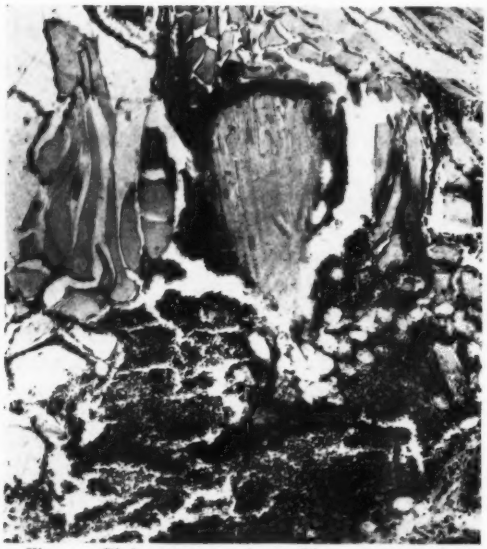

Fig. 1. *Plain catgut—3 days.* The catgut—in lower center—is surrounded by numerous polymorphonuclear cells. Elsewhere there are innumerable polymorphonuclear leucocytes and large quantities of necrotic muscle. The surrounding tissue is edematous, and fibrin is present.

Fig. 2. *Chromic catgut—5 days.* In this photomicrograph there is noted marked polymorphonuclear leucocytic infiltration around the sutures. Fibroblasts and lymphocytes are observed in the vicinity but the collagen is but scanty.

Fig. 3. *Plain catgut—8 days.* There is present much fibrosis here, but the fibroblasts and the collagen are, for the most part, of a young type. The dark, fragmented area represents numerous polymorphonuclear leucocytes and a moderate number of red cells.

laries. Small scattered areas of necrosis with collections of polymorphonuclear cells about them and small abscess formations are seen, limited for the most part to the muscle.

On the 2d postoperative day the sutures are intact with small abscesses about them. Collagen is not present. One section shows a minimal number of young fibroblasts. Previously existing capillaries show moderate en-

TABLE XIX.—POSITIVE WOUND CULTURES IN RELATION TO SUTURE MATERIAL[1]

Suture material	No. of animals	No. of cultures taken	Positive cultures		Organisms recovered
			No.	Per cent	
Catgut	66	60	12	20	Staphylococcus aureus, nonhemolytic streptococcus, pyocyaneus, colon bacillus
Silk	56	56	4	7.1	Staphylococcus aureus, nonhemolytic streptococcus
Cotton	56	43	2	4.7	Nonhemolytic streptococcus
Wire	55	51	4	7.8	Staphylococcus aureus, nonhemolytic streptococcus
Nylon	55	55	4	7.3	Staphylococcus aureus

[1]Tables 1 to 18 in previous issues.

Fig. 4. *Plain catgut—13 days.* The compact fibers are surrounded by an edematous, vascular granulation tissue, in which many fibroblasts and much of the collagen are of the young type. Adult types of each are also present. There are numerous lymphocytes and histiocytes.

Fig. 5. *Chromic catgut—31 days.* The granulation tissue by which the catgut is surrounded is composed for the most part of adult fibroblasts and strands of dense collagen. It is moderately vascular, and numerous histiocytes and a moderate number of lymphocytes are present. A few polymorphonuclear leucocytes are present in between the fragments of the suture material.

gorgement. Only a small number of chronic inflammatory cells are noted. Scattered abscesses are present, and there are areas of necrosis in the muscle and fascia.

On the 3d day sections show a minimal degree of edema. Small amounts of fibrin are present. There are large collections of polymorphonuclear cells about the sutures. Some young fibroblasts are seen, and collagen is young and slight in amount. In one section (205) a few thick strands of mature collagen are noted, and capillary buds are seen in the area of fibroplasia. Elsewhere only a few capillary buds are noted, and pre-existing capillaries are only slightly dilated. Some chronic inflammatory cells are present. Scattered small abscesses, small areas of necrosis in the muscle and fascia, and a few focal hemorrhages are observed.

On the 4th day edema is marked and larger amounts of fibrin are present. Beginning fragmentation of the sutures is noted with abscess formation about them. Some young fibroblasts are seen, collagen production is minimal, and the collagen is immature. Vas-

Fig. 6. *Chromic catgut—62 days.* The fragments of suture material are surrounded by fibroblasts, lymphocytes and histiocytes. Collagen is of the dense, adult type.

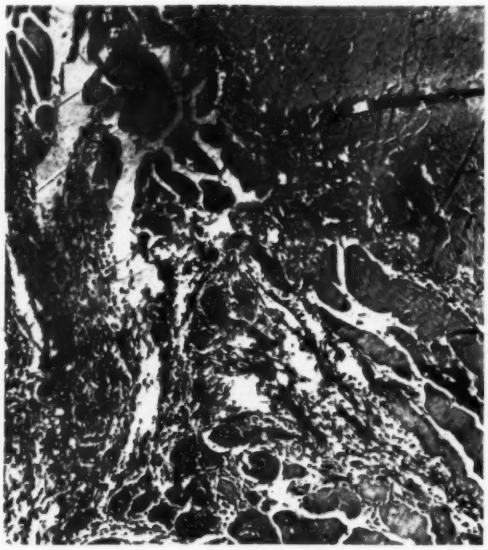

Fig. 7. *Silk—3 days.* The suture material—dense black strands—is embedded in an area of moderate edema and lymphocytic infiltration. The fibroblasts are for the most part of a young type, and there is scanty collagen present.

Fig. 8. *Silk—5 days.* Here, the silk, represented by the black homogenous material and the tissue defect, is ringed by both young and mature fibroblasts, numerous lymphocytes, a few histiocytes, and scattered capillaries. Much of the abundant collagen is of the adult type.

cularity is moderate and capillary buds are forming. There is a diffuse infiltration of chronic inflammatory cells, and there are some large mononuclear cells. The acute inflammatory process is diffuse and there are many abscesses and areas of necrosis. A few small focal hemorrhages are present. In wounds sutured with chromic catgut a number of young fibroblasts and a few mature fibroblasts are present. Collagen is a little more abundant and a few areas of maturing collagen are noted.

On the 5th day a number of mature and young fibroblasts are present. Young and mature collagen is present in about equal amounts. Many new capillaries are seen. Chronic inflammatory cells are diffuse throughout all sections. Acute inflammatory reaction and many small abscesses are seen. There are scattered small areas of necrosis, particularly in the muscle, and a large area of necrosis about one suture. In the reactive areas, small focal hemorrhages and thrombosis of small blood vessels are noted. In the chromic catgut sutured wounds the number of mature fibroblasts is greater and strands of collagen are beginning to appear.

Suture material on the 6th day is largely fragmented; there are a few polymorphonuclear cells with little fibrin and a few mature fibroblasts about it. Fibroplasia is increasing. The majority of the fibroblasts are young and immature. Collagen is present in moderate amounts and is mostly precollagen, although some is mature collagen. Many young capillaries are noted. Chronic inflammatory cells infiltrate the wound. A few small necrotic areas are seen, surrounded by small abscesses.

By the 7th day only small fragments of suture material remain, surrounded by collagen and young fibroblasts. Fibroplasia is marked, and the majority of the fibroblasts are mature. Collagen is abundant, mature, and arranged in bundles. Vascularity is marked. Chronic inflammatory cells are seen throughout all sections. There are abscesses about small areas of necrosis in the muscle and about the suture fragments.

On the 8th day edema is slight and only small amounts of fibrin remain. Sutures are

Fig. 9. *Silk—8 days.* Suture material is invaded and surrounded by numerous fibroblasts, many of adult form. The collagen is dense. Numerous lymphocytes, a few histiocytes, some giant cells are present. There are fibroplastic invasion of bundle of silk and some altered muscle in upper right.

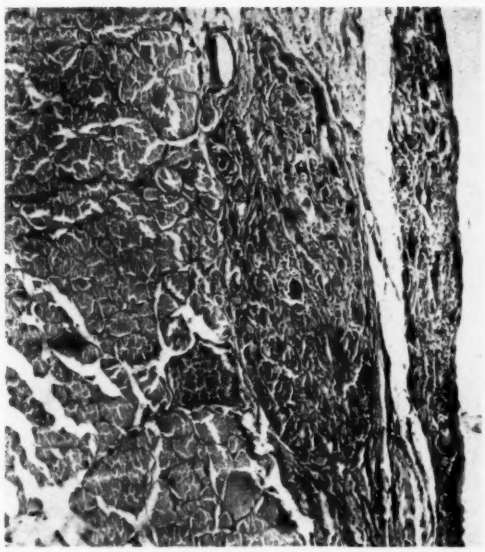

Fig. 10. *Silk—45 days.* Many of the fragments of suture material in this section are engulfed by giant cells, and the entire area is invested by fibroblasts and some lymphocytes. A few dense strands of collagen are seen throughout the area.

present only as fragments, with a collection of polymorphonuclear cells and fibroblasts about them. Some mature fibroblasts are present, collagen is mostly adult, marked in quantity, and bundles are frequent. Vascularity is decreasing, and acute and chronic inflammatory cells are diffuse throughout the sections. Necrosis is slight in the muscle and abscesses are not seen.

The picture on the 9th day is similar to that on the 8th, except that collagen is more dense. Areas of necrosis and small abscesses are seen.

By the 13th day edema and fibrin have disappeared. Only small fragments of suture material remain, more plentiful in the chromic section than in the plain. Giant cells and fibroblasts are seen about the sutures. Fibroplasia is marked and the fibroblasts are adult. Collagen is dense and mature. Chronic inflammatory cells are fewer in number and the acute inflammatory process has subsided except for scattered minute abscesses associated with residual necrosis in the muscle.

On the 21st, 31st, 45th, and 62d days edema, fibrin and suture material are not recognizable. Fibroblasts are old, collagen is dense and mature. A few old capillaries are seen, and the acute and chronic inflammatory reaction has completely subsided. In chromic catgut sutured wounds, however, a few fragments of suture material remain with small collections of polymorphonuclear cells about them. There is also a diffuse chronic inflammatory reaction and large phagocytes may be seen about the sutures.

Silk. Free serum was rarely seen in silk sutured wounds. Occasionally, some fibrinopurulent exudate was seen along the suture line.

On the 1st postoperative day, sections showed some edema and fibrin. Polymorphonuclear cells are seen around the suture and in one section a small abscess is present. Fibroblasts and collagen are absent with the exception of a few young fibroblasts in one section. The old capillaries are moderately dilated. Acute inflammatory cells are present only about the suture material, and a few scattered chronic inflammatory cells are

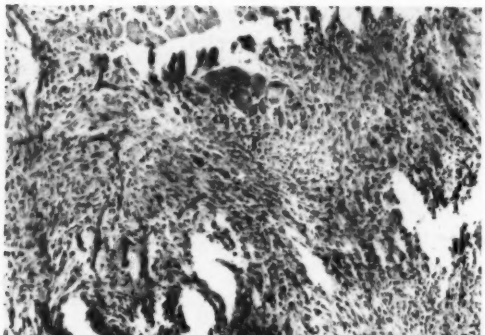

Fig. 11. *Wire—5 days.* The white space represents the tissue defect left behind by the removed wire. About it, the fibroblasts are of the young type, as is the pale, light pink fibrillar collagen. A few lymphocytes and histiocytes are present. There are plump, fusiform fibroblasts (young), and early collagen (pale, fibrillar, light pink), but no acute reaction.

noted. Small areas of necrosis are seen in juxtaposition with the incision and in one slide an area of necrosis is seen in the muscle. There are a few scattered hemorrhages.

On the 2d day a few young fibroblasts and some immature collagen are seen in all the sections. Vessels are engorged, and a few young capillaries may be seen. Acute and chronic inflammatory cells are scattered throughout the section. An increased number of polymorphonuclear cells are seen about the suture and in the small necrotic areas in the muscle. No abscesses are in evidence. Scattered hemorrhages are present.

Sections on the 3d postoperative day show that the suture material is beginning to split. A few polymorphonuclear cells are seen about and among the strands of the suture material. A few immature fibroblasts, some immature collagen and a few young capillaries are noted. In the case of animal No. 340 fibroplasia and collagen formation are more marked. A hematoma is present and in this area there is a collection of polymorphonuclear cells and some muscle necrosis. Wounds in other animals show only a few chronic and acute inflammatory cells and scattered areas of muscle necrosis.

The 4th day shows invasion of the suture by a few young fibroblasts, most of them immature, collagen is practically all immature, although some maturing islands are noted. A number of young budding capillaries are seen. There are no abscesses and chronic and acute inflammatory infiltration is slight. A few scattered hemorrhages and small areas of muscle necrosis are noted.

On the 5th day, section shows the suture material invaded by chronic inflammatory cells including a few giant cells. A few polymorphonuclear cells are seen about the suture material and invasion by young and mature fibroblasts is well under way. A considerable amount of mature collagen and many capillaries are seen. Acute inflammatory reaction is slight and no abscesses are seen. In the case of animal 343 muscle necrosis is marked and here polymorphonuclear cells have gathered. There are some very small hemorrhages.

By the 6th day fibrin is no longer recognized. The suture material is invaded by many fibroblasts, most of which are mature. Mature collagen is present, but most of it is intercellular and bands have not yet started to form. Chronic inflammatory cells and a few giant cells are present. Only a few polymorphonuclear cells are noted, and there are no abscesses, necrosis, or hemorrhage.

Sections on the 7th postoperative day show that large numbers of fibroblasts have surrounded and infiltrated the suture fragments. Fibroplasia has increased and the majority of the cells are mature. Mature collagen is present in large amounts and in some areas is arranged in dense bundles. Vascularity is mild and only a few acute and chronic inflammatory cells are seen. There are no abscesses, areas of necrosis, or hemorrhage.

The 8th and 9th days present a similar picture except that more giant cells are noted, and there are fewer chronic inflammatory cells. Collagen is present in dense strands, the fibroblasts are mature.

From the 13th to 21st day only few chronic inflammatory cells are seen. Scars are dense.

Sections on the 31st, 45th, and 62d postoperative days show dense scar tissue, in which the suture material is embedded. Occasional giant cells are seen.

Wire. Grossly, only an occasional wound showed a small amount of fibrinopurulent exudate. No serum was observed.

Sections were not taken through the sutures.

On the 1st postoperative day section shows moderate edema and a small amount of fibrin. Fibroblasts and collagen have not appeared. Except for small focal collections of polymorphonuclear cells surrounding minute areas of necrosis in the muscle, no reaction was observed.

On the 2d day edema and fibrin are increased. A few immature fibroblasts, small areas of young collagen, and a few capillary buds are recognized. Chronic inflammatory cells are few and scattered. A few small hemorrhages are seen.

On the 3d day fibroblasts are increased in number, but they are young and immature. Collagen formation is immature. Polymorphonuclear cells are less numerous than on the 2d day although in one section (animal 426) a small abscess is noted. Lymphocytes and mononuclears are numerous, and diffusely arranged. Scattered areas of necrosis are noted, and vascularity is characterized by budding capillaries.

By the 4th day many fibroblasts are present, most of which are young. Collagen, although increased in amounts, continues young and intercellular. Some young capillaries are present and chronic inflammatory cells and occasional giant cells are diffusely spread throughout the section. Acute inflammatory cells are few in number except in the case of animal No. 435 which presents a fairly large area with central necrosis, surrounded by polymorphonuclear cells. Some muscle regeneration is noted. There are a few very small focal hemorrhages.

Sections on the 6th and 7th days show fibroblasts numerous and mature and collagen maturing rapidly. Some new blood vessels are seen. Chronic inflammatory cells and giant cells are present in considerable numbers but are diffuse. No hemorrhages are seen.

Fig. 12. *Wire—8 days.* The fibrous tissue here is composed of numerous fibroblasts, mostly of the adult type, a moderate amount of fairly dense collagen, and but a few lymphocytes.

On the 7th and 8th days a large number of mature fibroblasts may be seen. Strands of adult collagen are noted. The acute inflammatory reaction has subsided except in the case of animal No. 419 which presents an abscess surrounding a large area of necrosis in the muscle. Blood vessels are more mature. By the 8th day the abscess and necrosis have disappeared.

The 9th postoperative day shows fewer fibroblasts, but collagen is dense and mature and is arranged in bundles. Few blood vessels are seen and they are of the adult type. No necrosis or inflammation can be seen.

By the 62d day edema and inflammation have completely subsided. The scar is adult.

Cotton. On the first postoperative day sections show edema and fibrin, particularly in the fascia and the peritoneum. There are collections of polymorphonuclear cells surrounding the suture and between its strands. No fibroblasts or collagen are seen. Previously existing capillaries are dilated and engorged. There are a few small areas of necrosis. On the 2d day there is noted the beginning of a

Fig. 13. *Cotton—3 days.* There is a small collection of polymorphonuclear leucocytes adjacent to the suture. The tissue about the cotton is moderately edematous, diffusely infiltrated with a few polymorphonuclear leucocytes and a moderate number of lymphocytes, and vascular. The fibroblasts are of the young type, and the collagen is rather scanty in amount, and of the pale, fibrillar young form.

Fig. 14. *Cotton—5 days.* There is very little acute reaction. Fibroblasts are equally divided between young and old forms. Collagen is scanty but nearer the mature type of collagen. There are a few lymphocytes and histiocytes.

diffuse infiltration of chronic inflammatory cells and in two sections, a few fibroblasts of the young, immature type.

On the 3d day many young fibroblasts are noted, and some immature collagen. New capillaries are present. Chronic inflammatory cells are diffuse throughout the sections, particularly in areas with engorged channels, believed to be dilated lymphatics. Acute inflammatory cells are restricted to the areas containing the sutures and surrounding several small areas of necrosis in the muscle. Here small focal hemorrhages are found.

On the 4th day only a few polymorphonuclear cells are seen, and young fibroblasts surround the sutures. Collagen is abundant, and for the most part, immature. Some young capillaries are seen. Chronic and acute inflammatory cells are few and diffusely arranged. No abscesses or areas of necrosis are seen. In one section (118) there is a hemorrhagic area, greater edema and deposition of fibrin, fewer fibroblasts, and less collagen.

Sections on the 5th postoperative day show large numbers of fibroblasts surrounding the sutures and among the strands. Fibroplasia is greater and an increasing number of mature cells are seen. Strands of mature collagen are discernible in many areas. Some young capillaries are noted. A few chronic inflammatory cells and a few polymorphonuclear cells are scattered throughout. In one section (259) a small abscess is seen surrounded by excessive edematous granulation tissue and many polymorphonuclear cells. A few minute focal hemorrhages are present.

On the 6th and the 7th days the picture is similar to that on the 5th day, except that fibroblasts are mature and collagen is abundant and dense. Section 252 shows a central abscess surrounding necrotic muscle. On the 7th day section 112 shows a large abscess about an area of necrotic muscle surrounded by edematous granulation tissue and many polymorphonuclear cells.

On the 8th day the sutures are surrounded and invaded by fibroblasts. No inflammatory cells, edema or fibrin, are present. A few im-

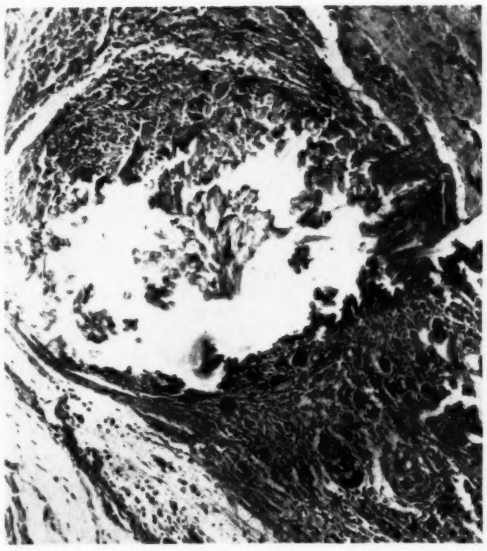

Fig. 15. *Cotton—13 days.* Here, not only the entire suture, but each individual fiber is invested by adult fibroblasts and foreign body giant cells. Lymphocytes and histiocytes are also present. Acute reaction is minimal. Collagen is of the adult type, although not yet as dense as seen in older sections.

Fig. 16. *Cotton—31 days.* Each fiber is surrounded by fibroblasts, and relatively numerous lymphocytes and histiocytes. A few giant cells are present. Collagen is scanty, and consists of a few dense fibers. No acute reaction is present.

mature types of fibroplasia persist. Collagen is dense, of the adult type, and laid down in strands. Some chronic inflammatory cells and a few foreign body giant cells are diffused throughout. Acute inflammatory reaction is very slight.

By the 13th day the sutures are seen to be embedded in fibroblasts, and a few chronic inflammatory cells and giant cells are seen surrounding them. There is no evidence of acute inflammatory reaction. Section 240 is overrun with polymorphonuclear cells showing edema. There are numerous young capillaries and the blood vessels are dilated.

On the 21st day, fibroblasts, although adult and abundant are not as dense as might be expected at this stage. Foreign body giant cells are seen about the sutures.

By the 62d day dense strands of collagen have formed. There is no inflammatory reaction. Foreign body giant cells are present about the suture material.

Nylon. Sections from nylon sutured wounds on the 1st postoperative day show edema and

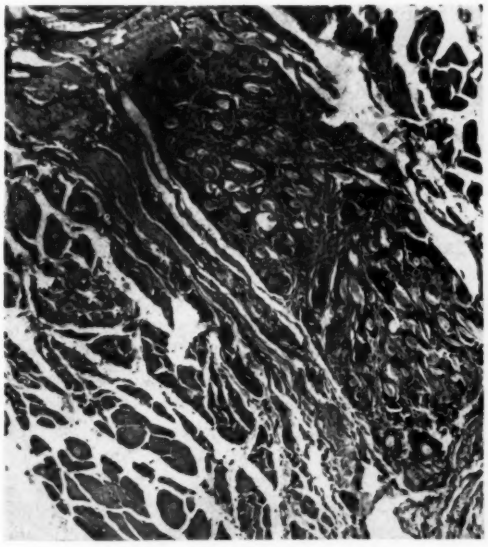

Fig. 17. *Cotton—62 days.* There is a compact mass composed of cotton fibers, each of which is ringed by fibroblasts and dense collagen. Histiocytes and lymphocytes are sparsely scattered about and a few giant cells are present.

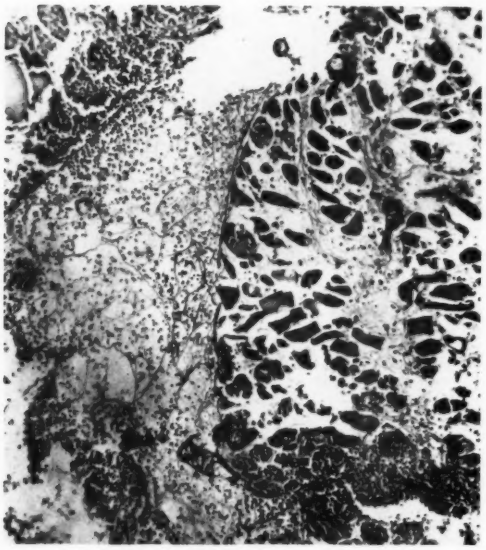

Fig. 18. *Nylon—1 day.* In this specimen there is noted marked edema, much fibrin, a few necrotic muscle fibers, and a moderate number of polymorphonuclear leucocytes.

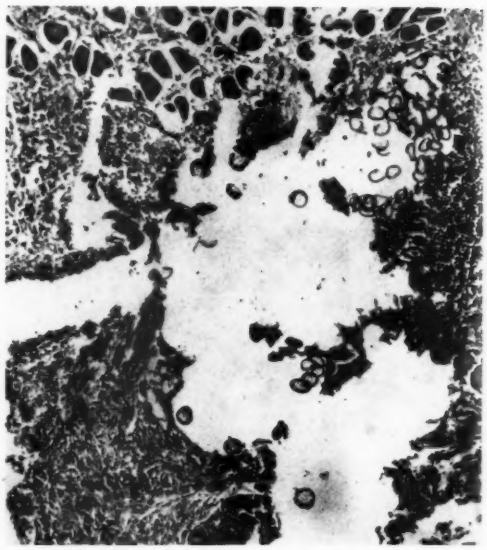

Fig. 19. *Nylon—3 days.* There is a collection of polymorphonuclear leucocytes near suture material. Nearby tissue is edematous, vascular, and the fibroblasts are of both young and adult form. Collagen is scanty, fibrin present.

deposition of fibrin. A few polymorphonuclear cells surround the suture material. Some acute and chronic inflammatory cells, and several small hemorrhages are present.

On the 2d day edema and fibrin deposition have increased. Collagen and young fibroblasts are not seen. A few capillary buds are present. A few chronic inflammatory cells are scattered throughout and acute inflammatory cells are present in small groups surrounding small areas of necrotic muscle, forming small abscesses.

On the 3d day some young fibroblasts and capillaries are seen, and a small amount of young collagen is present. There are a few chronic inflammatory cells and a few polymorphonuclear cells about the suture material. Section 382 shows more collagen and more advanced fibroplasia. On the 4th day sections show scattered focal hemorrhages. Many areas of muscle are altered although not necrotic.

Edema has decreased by the 5th day. Fibroblasts and collagen are more abundant and maturing. Fibroblasts are seen around and in the strands of the suture material.

On the 6th day mature collagen is laid down in thick strands. In animals 391 and 376 there are areas of muscle necrosis with abscess formation surrounding them. Animal 376 also shows a distinct retardation of fibroplasia as compared with other animals in this group.

By the 7th day edema has practically subsided although fibrin fragments are still recognized. The sutures are embedded in fibroblasts which are abundant and of the adult type. Collagen is laid down in dense mature strands. A few adult capillaries are present. Chronic inflammatory cells are scattered, the acute inflammatory reaction has subsided and only a few polymorphonuclear cells are noted. Areas of regenerating muscle are seen.

On the 9th day the scars present mostly mature fibroblasts and thick bands of mature collagen. Animal 358 shows a cavity filled with granulation tissue and containing a small number of polymorphonuclear cells. By the 13th day the inflammatory reaction and edema have subsided. The scar is adult in type and cellular. By the 62d day the scar is contracting and is less cellular. The suture

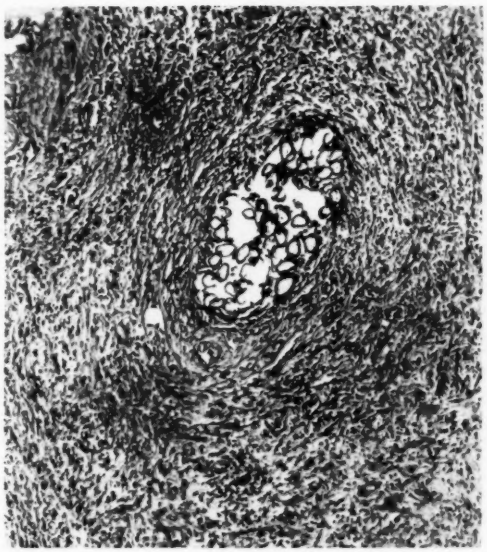

Fig. 20. *Nylon—5 days.* The bundle of nylon is well surrounded by fibroblasts, many of which are of the adult type. The collagen is abundant, and much of it, while not dense, is well on its way to the adult form. Lymphocytes and histiocytes are slight to moderate in number, and a few capillaries are present. There is slight edema.

Fig. 21. *Nylon—8 days.* The collagen is relatively abundant and dense; the few fibroblasts are of the adult or slightly younger type. There are a few lymphocytes, histiocytes and foreign body giant cells. Edema is present but is only slight. There is very little inflammatory reaction.

material is embedded in scar tissue and a few giant cells are seen surrounding it.

SUMMARY

Grossly, little difference was observed among wounds sutured with nonabsorbable materials. Serum was not seen in large amounts in cotton, silk, wire, or nylon sutured wounds. Furthermore, it was unusual to find serum in the subcutaneous tissues after the 3d or 4th day in animals whose wounds were sutured with nonabsorbable material.

Catgut sutured wounds, on the other hand, contained serum in varying amounts up to the 9th day. The wounds were pale, and a fibrinopurulent membrane was present along the fascial and peritoneal suture line between the 2d and the 7th day. Very few of the wounds sutured with nonabsorbable material showed this membrane and only between the 2d and the 4th day.

Microscopically, marked differences are seen between catgut sutured wounds and those sutured with the nonabsorbable materials. Catgut wounds show edema for longer periods of time and maturation of fibroblasts and collagen is retarded (Figs. 1, 2, 3, 4, 5, 6). The most significant difference is in the inflammatory reaction. In catgut wounds it is acute, intense, prolonged, and associated with widespread death of tissue and abscess formation.

Among the wounds sutured with nonabsorbable materials, no significant histopathological differences were noted. Fibroplasia, collagen formation, and maturation are practically the same in the case of all materials (Figs. 7 to 21). In silk and cotton sutured wounds the inflammatory reaction is somewhat more intense and prolonged than in the case of nylon and wire sutured wounds (Figs. 7, 8, 9, 10, 13, 14, 15, 16, 17). Healing occurs at about the same rate. Studies of tensile strength agree with these observations.

Little difference in tensile strength was observed between wounds sutured with plain catgut and those sutured with chromic catgut, although mature fibroblasts and collagen

were noted 1 day earlier in chromic catgut sutured wounds.

It is of interest to note that fragments of chromic catgut are observed in wounds at the end of 2 months and that an inflammatory reaction is still present about the suture material at this time (Fig. 6). Wounds sutured with nonabsorbable sutures also show the material present at the end of 2 months but it is fragmented and encapsulated by fibroblasts, and shows evidence of a foreign body reaction (Fig. 17).

Two factors are apparently responsible for the prolonged lag period in healing observed in catgut sutured wounds: first, the marked destruction and acute inflammation (Figs. 1 to 6) which necessitate a prolonged period of débridement; second, the delay in the maturation of fibroblasts and collagen, due probably to acute inflammatory reaction. The delay in final healing of catgut sutured wounds, as noted in studies of tensile strength, and also microscopically, must be attributed to the more widespread destruction and acute inflammation of tissues in these wounds.

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HORIZONTAL PIN FIXATION FOR FRACTURES OF MANDIBLE USING PIN GUIDE

DOUGLAS F. PINCOCK, D.D.S., Major, D.C., A.U.S., Ogden, Utah

MANY professional articles as well as those for the layman have been written concerning fracture appliances which permit function during healing. It is a recognized fact that normal physiological function must be limited to some degree. However, any use that can be made of a reduced fracture during treatment is a distinct advantage.

There have been many methods of treating fractures of the mandible, all having advantages and disadvantages. Interdental immobilization by wiring is a simple method, quickly applied, but does not permit mandibular motion or facilitate good oral hygiene. The use of intraoral splints permits mandibular motion but prevents proper cleansing of the area involved. Extraoral appliances (Stader splint) is not the answer to most civilian fractures because cleansing and caring for the face is very difficult under this appliance. There are many advantages in its use, however, particularly in cases in which there has been a loss of bone (war wounds), and it is desired to maintain space, limiting the deformity and simplifying the reconstructive surgery.

It was in an effort to find some means of fracture fixation that would permit mandibular motion and good hygiene that the horizontal pin method was devised. This procedure consists of one or two pins (Kirschner wire, large) drilled horizontally through the body of the mandible, across the fracture with both ends of the pin imbedded in the cortical bone. The wire can be cut short and the skin raised over the end, leaving no external evidence of the fixating pin.

This type of fracture immobilization permits normal physiological mandibular function. The patient is able to continue with his work, carry on a regular routine of life, being limited only to a liquid or soft diet.

From the Oral Surgery Section, Hoff General Hospital, Santa Barbara, California.

After having drilled a few of these pins in the mandible, one is soon convinced of the necessity of some type of a pin guide. I designed and had Jack Pava, brace mechanic at Hoff General Hospital, make the pin guide shown in Figure 1. The tube *A D* directs the wire to point *B*. This device eliminates the guesswork and hazards of freehand drilling.

The technique used is as follows: A minimum of loop wires is applied to the upper and lower teeth. Intermaxillary rubber bands are used to re-establish proper occlusion and alinement of the fragments. This is a very important step. If normal interdental relation is not correctly established, the resulting malocclusion will produce traumatic pressures with the resulting loosening of the pin and possible failure of union. Block anesthesia is used with local infiltration in the region of the symphysis and posterior border of the mandible. The pin guide is applied by first inserting the point *B*, Figure 1, into the posterior border of the mandible. The point of the guide tube (*A*, Fig. 1) is then positioned into the area lateral to the symphysis. The wing pin (*C*, Fig. 1) is then tightened as the pin guide is rotated on its axis (*A B*, Fig. 1). These points are so beveled that they will drill themselves into the cortical bone. When the pin guide is firmly clamped into position, posteroanterior, and lateral jaw x-ray films are taken. This permits checking the position of the director before the pin is drilled into the mandible. The pin is then screwed out of the tube at *D*, Figure 1, and the large Kirschner wire is run through the directing tube and drilled into position. It is necessary to disassemble the two halves of the clamp by releasing the wing pin to remove it from its position. Digital examination is then made to find the posterior end of the pin. If it cannot be located, the drilling is continued until the end can be felt just through the posterior border of the ramus. The pin is cut short

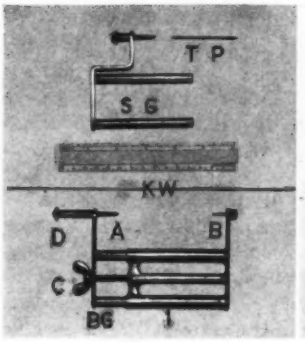


Fig. 1.

Fig. 2.

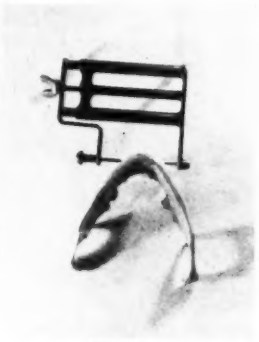


Fig. 3.

Fig. 1. *A* and *B*, Tribeveled points; *D*, Thumb nut and pin which when removed opens tube *D-A*; *C*, wing bolt for clamp adjustment; *B-G* and *1*, mandibular body guide (see Fig. 2); *S-G* substituted for *B-G* with *1* makes symphysis guide (see Fig. 3); *K W*, Kirschner wire (large); *T-P*, threaded pin (stainless steel) .081 by 58 mm.

Fig. 2. The body guide applied to the mandible (inferior view).

Fig. 3. Symphysis guide applied to mandible (inferior view).

enough to permit pulling of the skin and subcutaneous tissue over it. A small dressing is applied over the anterior and posterior pin holes in the skin and removed in 2 or 3 days. The mandible is subsequently roentgenographed to check the pin position, and then the interdental wires and rubber bands are removed. If it is felt that additional support is necessary to prevent rotation of the fragments, a figure of eight wire can be applied to the teeth on either side of the fracture.

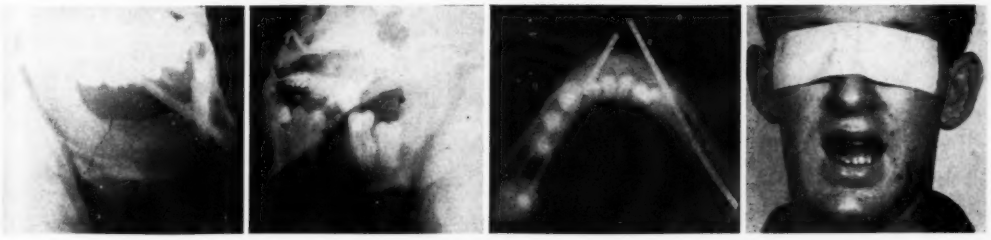
The pin can be removed in about 6 weeks under local anesthesia. The end of the pin is located by digital examination, and about 1 cubic centimeter of 2 per cent procaine is infiltrated into the area. The operator makes a small stab incision, feeling the end of the wire with the scalpel. The surrounding tissue is compressed until the end of the pin extends through the incision. It is grasped in a heavy plier and withdrawn by a rotating motion.

Figs. 4 and 5. Case 1.

It has been rather surprising how firmly the pins have been held in position, and at times they require considerable turning to free them.

A series of twelve completed cases have been treated in this manner at Hoff General Hospital, U. S. Army. We have had no infections, and all have healed with excellent results. The patients have been very comfortable during treatment, and a casual observer would not know they were being treated for mandibular fractures. In fact, I have had 2 patients ask for this form of treatment. They were patients with interdental wiring applied at their station hospitals, then transferred to our hospital, and were able to observe this type of fixation on other patients in their ward. When patients ask for it, the factor of comfort must be of some importance.

CASE 1. C. A., age 29 years; diagnosis: fracture of the mandible, ununited, oblique, region of the right symphysis, with overriding edentulous fragments. Injury sustained in automobile accident 13 years prior to entrance into military service. General anesthesia—nitrous oxide oxygen and ether was used and open reduction was carried out. An incision was made along the inferior border of the mandible over the fracture site, and the periosteum was reflected from the fragments. The ends (two) were freshened by means of an electrically-driven circular saw. The fragments were then approximated and held in position by two crossed horizontal pins (threaded .081 stainless steel). The periosteum and subcutaneous tissue were approxi-



Figs. 6, 7, 8, 9, from left to right. Case 2.

Figs. 10, 11, 12, from left to right. Case 3.

mated with catgut; the skin was sutured with 5.0 silkworm gut (Figs. 4 and 5).

This patient had an uneventful recovery. The pins were removed 8 weeks after operation under local anesthesia. The fragments were healed in excellent position, and the patient was returned to full duty.

CASE 2. K. E. J., aged 29 years; diagnosis: fracture of mandible, compound, comminuted, complete, bilateral, regions of left 1st molar and right 3d molar, accidentally incurred during supervised athletics.

The anesthesia was produced by mandibular block, with local infiltration. A minimum of looped wires was applied to the teeth, and intermaxillary rubber bands were used to re-establish the occlusion and alignment of the fragments. The pin guide was applied and adjusted into position. A large Kirschner wire was drilled horizontally through the body of the right and left mandibles. A figure-of-eight wiring was applied to the teeth, left, 1st and 2d bicuspids and 1st molar, to aid in preventing rotation of the fragments (Figs. 6, 7, 8).

This patient had an uneventful recovery. The pins were removed in 6 weeks, and the soldier returned to full duty.

CASE 3. P. S. I., aged 22 years; diagnosis: fracture of the mandible, compound, comminuted, complete, unilateral, region of the left 2d molar. The fracture was sustained during a fight with another soldier.

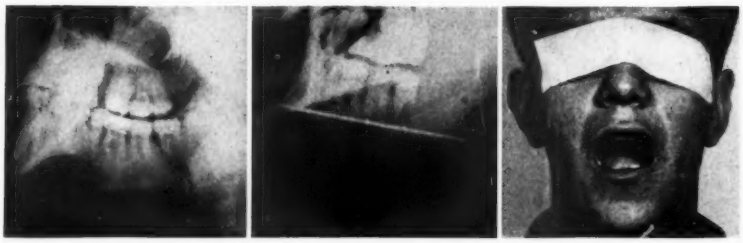
Mandibular block, with local infiltration anesthesia was used. Occlusion was re-established and the fragments were realined by the use of the loop method, with intermaxillary rubber bands. A Kirschner wire was drilled from the posterior border of the ramus anteriorally, making its exit on the lateral surface of the mandible in the region of the mental foramen. The wire was directed in this position by inserting point *A*, Figure 1, of the pin guide, into the posterior border of the ramus, and point *B*, Figure 1, held into the lateral surface, just above the inferior border, in the region of the mental foramen. This mandible was oval in shape, the patient's face being very round, making it impossible to drill the wire from the symphysis to the posterior border of the ramus (Figs. 10, 11, 12).

There were no complications, and the pin was removed 6 weeks after operation, under local anesthetic. He was returned to full duty the following week.

CASE 4. A. T. S., aged 19 years; diagnosis: fracture of the mandible, compound, comminuted, complete, unilateral, region of the left 1st molar. Patient was injured when he was struck on the jaw by a civilian. The anesthetic used was mandibular block, with local infiltration. Occlusion was re-established by the loop method and intermaxillary rubber bands. The pin guide was applied, and a Kirschner wire (large) was drilled horizontally through the body of the mandible, extending from the left symphysis to the posterior border of the ramus (Figs. 13, 14, 15).

The pin was removed in 6 weeks, and the soldier was returned to duty 4 days later. There were no complications during treatment of this case.

The method of treating fractures of the mandible was thought to be new and was so demonstrated at the October 19, 1942, staff



Figs. 13, 14, 15, from left to right. Case 4.

meeting of the Hoff General Hospital, U. S. Army. However, articles were later found dating the treatment as early as July 9, 1932 (2), and Sobye (4) published a series of 25 cases in 1939. This treatment was also reported by Meade (3) in 1935 and Brown (1) in 1942.

These articles have all reported a tendency of the pin to loosen after operation. This has not been the experience at this hospital. The pins removed 6 weeks after operation seem to offer about the same resistance as those which were removed for redrilling. If the pin is confined to the intermedullary bone, the loosening is negligible. The pictures demonstrated in the articles by Ipsen, Meade, and Sobye give one the impression that the pins have been drilled from the right to the left mandibles, across the floor of the mouth. It is possible that the muscle traction in the floor of the mouth accounts for the reported loosening of the pin.

The question might well be asked: What will happen to the mandibular nerve if the pin is drilled into the canal? An effort is made to place the pin below the canal, but if the Kirschner wire should enter it, I believe it to be of no importance. The wire is smaller in diameter than the canal, and as the pin passes through the canal, the nerve will be pushed aside, causing little or no damage.

It is very difficult to judge the trauma associated with drilling the pin in the canal because of the anesthesia usually present with mandibular fractures. In the series of patients treated at this hospital, it has been impossible to observe any change in the degree of anesthesia. Four of the postoperative x-ray films have shown the pin and mandibular canal in contact. However, one must keep in mind that the pin could be placed in a position medial or lateral to the canal, and the shadows superimposed. Therefore, the pin may or may not have been drilled into the canal.

CONCLUSION

Positioning the horizontal pin or Kirschner wire (large) through the mandible requires accurate drilling. The pin guide will direct the wire into only one position, points *A* and *B*, Figure 1. Therefore, the success in positioning the pin correctly depends upon the proper adjustment and alinement of the guide.

ADVANTAGES

The comfort of the patients is a paramount factor. They are able to keep their mouths clean, to eat without the laborious effort of sucking everything through their teeth, and to speak distinctly. In other words, the patient has normal physiological mandibular motion, being limited only to a liquid or soft diet. There is no external appliance to interfere with the cleaning of the face and to detract from the appearance of the patient.

The only disadvantages of this method, compared to intraoral immobilization, is that this procedure must be done aseptically and requires an operating room to carry out the technique.

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PROTRUDED INTERVERTEBRAL DISKS

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INTERVERTEBRAL disks are the fibrocartilaginous shock absorbers that normally are placed between the bodies of the movable vertebrae of the spinal column. By protrusion of a disk we mean an abnormal posterior displacement of a portion of that disk. We believe that this, to be of significance, has to be associated with a fragmentation of the fibrocartilage. That is, the continuity of the disk is interrupted and one or more fragments are displaced posteriorly so as to be capable of causing undue stretching or tearing of the posterior longitudinal ligament which forms the anterior wall of the spinal canal. In addition to the abnormal pressure on, or rupture of, this ligament there is usually associated intraspinal irritation of, or pressure on, nerve roots if the lesion is in the lumbar portion of the spinal canal or pressure on the roots or the spinal cord itself if the lesion happens to be in the cervical or thoracic portion of the spinal canal.

Although protruded intervertebral disks as such have been recognized and their clinical importance has been established only since the excellent work of Mixter and Barr, the condition was found occasionally at operation when patients were subjected to laminectomy for a supposed intraspinal neoplasm as long ago as 1922, when Adson encountered several of the lesions and considered them to be primary cartilaginous neoplasms or enchondromas.

Goldthwait, Adson, Dandy, Stookey, and others have contributed to our knowledge of this condition. In 1936 one of us (Love, 6) introduced the term "protruded intervertebral disk" as most appropriate for the condition. This designation has since been accepted by the *Journal of the American Medical Association* and by Dr. Mixter as quite satisfactory.

Today this lesion is accepted as a distinct clinical and pathological entity and all up-to-date textbooks of orthopedics and neurology should include a discussion of the condition.

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ANATOMY OF THE INTERVERTEBRAL DISKS

The intervertebral disks are fibrocartilaginous cushions which are placed between the vertebral bodies. They are bounded anteriorly by the anterior longitudinal ligament and posteriorly by the posterior longitudinal ligament. The intervertebral disks are applied to the surfaces of the cartilaginous plates which cover the bony vertebral bodies and normally they do not extend beyond the margins of the vertebral bodies. Under conditions of normal stress and strain they bulge slightly beyond these limits; but when the force exerted against the vertebral column or on it is no longer acting, the normal disk returns to its normal confines. The disk is composed of two structures: a central, loose, semigelatinous nucleus pulposus, in which is represented the remnant of the fetal notochord; and an outer, firmer, more fibrous annulus fibrosus.

PATHOLOGY AND ETIOLOGY OF PROTRUDED DISKS

As a result of our studies and those of Deucher and one of us (Love, 4) it is our opinion that the protruded portion of an intervertebral disk practically always consists of both nuclear and annular material. This is one of the reasons why we have adopted the term "protruded disk" as being more applicable than some of the others, such as herniated or extruded nucleus pulposus, rupture of the intervertebral disk with herniation of the nucleus pulposus, and so forth.

The protruded portion of the disk may show various degrees of degeneration and fragmentation, and the fragments may be very edematous at times. In the opinion of Deucher and one of us (Love, 4) this is due to a vascular change and this conclusion is supported by the fact that the nucleus pulposus is capable of increasing its volume many times when freed of the restraining influence of the annulus fibrosus.

It has become generally recognized that the protrusion of an intervertebral disk is often

preceded or accompanied by unusual stress or strain to the back. We have come to look on the condition as being definitely due to trauma. The injury may be relatively mild or severe. It may be direct or indirect. It is most often associated with the lifting of unusually heavy objects and the symptoms in their classic form may be sudden in onset or more or less gradual in their development. That there are predisposing factors we cannot deny but as yet there is no really clear-cut understanding of what they may be.

HISTORY TAKING IN CASES OF SUSPECTED PROTRUSION OF AN INTERVERTEBRAL DISK

In all diagnoses the patient's history constitutes one of the most important portions of the examination. This is particularly true in neurology and especially so in the diagnosis of protruded disk. The patient should be allowed to relate the story of the development and the progress of his disease. Leading questions should be avoided, particularly in dealing with patients who present a medicolegal problem and those of unstable or neurotic disposition. An occasional pertinent and pointed question while the patient is relating his story will serve to elucidate important points and to avoid an unnecessarily long record. There are several very important questions the answers to which should be obtained in the course of the history taking.

The patient's occupation and the type of work he usually does should be understood. Likewise, some information regarding his hobbies should be elicited. This is particularly true of golfers, hockey players, campers, canoers and horseback riders.

Did the pain—and pain is the cardinal symptom of protruded disk—of which the patient complains come on after an injury to the back, direct or indirect, after unusual lifting or stretching or being caught with the back twisted or in an awkward position? Had the patient been subject to backaches or "lumbago" before the onset of sciatic pain or pain of a lower extremity and did the sciatic pain come after unusual stress or strain? Is the pain constant or intermittent—and what, if anything, will give relief and what will aggravate it? The effect of coughing, sneezing, and straining at the stool should be determined. The results of various treatments, which the patient has usually tried, should be elicited. If scoliosis is not present at the time of examination the history of listing and particularly of alternating listing of the trunk is very important. The presence or absence of paresthesias in the distribution of the pain should be determined also. The patient should be asked as to his habits of sleep. If his sleep is disturbed by pain, the fact is significant. Twenty-seven per cent of 732 lumbar protrusions produced pain at night. It must be determined that the pain awakens the patient from his sleep rather than that for some other reason he wakes during the night and then becomes conscious of the fact that he is uncomfortable. Likewise, the history of loss of weight is important. Loss of weight is usually associated with loss of sleep and of appetite produced by pain. We have seen many patients in whose cases a malignant lesion has been suspected because of the loss of weight.

EXAMINATION OF THE PATIENT

Although the general physical examination of the majority of the patients suffering from protruded disk is found to be satisfactory for the patient of his particular age this part of the investigation should not be neglected if the risk of treatment is to be kept to a minimum. There is no reason, of course, why the patient cannot have other local or general diseases which might influence the treatment and even the diagnosis. If tuberculosis, bronchiectasis, diabetes, hyperthyroidism, hypertension, prostatism, pregnancy, obesity, Paget's disease, spondylitis, spondylolisthesis or any other disease is present, the fact should be noted and considered in the general summation of the problem and proper emphasis should be placed where it is indicated. There is no use in operating and removing a protruded intervertebral disk unless there is sufficient reason to believe that the patient will be materially benefited thereby and will not be subjected to an unwarranted risk.

In the course of the examination anteroposterior and lateral roentgenograms of the spinal column should be taken. In some cases oblique views also are necessary. Spondylitis,

tuberculosis of the spinal column, and metastatic and primary neoplasms of the spinal column should be excluded.

A competent orthopedic examination is essential and, if the opinion of a well trained orthopedist is sought, he may be able to recognize some osteopathy that has escaped detection. It is the practice in the clinic to have any patient in whose case there is suspicion of a protruded intervertebral disk examined by an orthopedic consultant before the patient is sent for a lumbar puncture.

The neurologic examination may in itself reveal enough positive findings to warrant the diagnosis of an intraspinal space-taking lesion; however, an accurate interpretation of those findings is dependent on a knowledge of the patient's history, the roentgenologic findings and those of the orthopedist. Without a knowledge of the fact that the patient's symptoms have been intermittent or that he suffered from backache for many years before a particular strain, which was followed almost immediately by paraplegia, a diagnosis of intraspinal neoplasm rather than of protruded intervertebral disk would be made. In many cases the neurologic findings are few and in some cases they are absent (Table I).

These statistics are founded principally on the results of our studies of the records of protrusions of lumbar disks, since protrusions of lumbar disks constitute by far the vast majority of the protrusions encountered and because if their origin, mode of involvement of nerve roots, type of symptoms produced, and so forth, are thoroughly understood, those protrusions occurring in other parts of the spinal canal can be recognized. The protrusions occurring in the cervical and thoracic portions of the spinal column present the symptoms and signs of an intraspinal neoplasm; more often than protrusions in the lumbar portion and unless there is a definite history of trauma preceding the onset of symptoms and unless the symptoms have been intermittent, it may be impossible to make the diagnosis until the lesion is uncovered at the operating table.

In all cases in which protrusion of an intervertebral disk is suspected, lumbar puncture should be performed and a careful analysis of a specimen of cerebrospinal fluid should be made. The most important information obtained is that relating to the presence or absence of a subarachnoid block and the amount of total protein contained in the fluid. It is rare to find a subarachnoid block associated with lumbar protrusions unless there is paraplegia, and it is infrequent that one finds a total protein content of more than 80 milligrams per 100 cubic centimeters of cerebrospinal fluid. If there is a subarachnoid block, a yellow fluid or a total protein content of more than 200 milligrams per 100 cubic centimeters, the presence of an intraspinal neoplasm should be suspected. We have encountered many unsuspected neoplasms among our cases in which protrusion of an intervertebral disk was suspected.

TABLE I.—NEUROLOGIC SIGNS IN 285 CASES OF PROTRUDED LUMBAR INTERVERTEBRAL DISKS

	Cases	Per cent
Positive Lasègue sign	231	81
Sciatic tenderness	172	60
Achilles reflex diminished or absent	171	60
Hamstring reflex diminished or absent	51	18
Muscular paresis	63	22
Sensory loss	62	22
Examination objectively negative	17	6
Examination objectively negative except for positive Lasègue sign or sciatic tenderness	42	15

INCIDENCE OF PROTRUDED INTERVERTEBRAL DISK

It is difficult or impossible to estimate the frequency of protrusion of intervertebral disks. In private practice this condition must account for only a very small percentage of the cases in which the physician is called on to treat backache and sciatic pain. The good results that most physicians obtain by conservative therapeutic methods would seem to confirm this. On the other hand, every physician who is called on to treat such conditions must occasionally encounter a pain that is intractable. It is from this latter group of intractable backaches and sciatic pains that the cases in which protrusion of a disk is suspected come.

The practice at the Mayo Clinic cannot be compared readily with that of the private physician, orthopedist, neurologist, or neurosurgeon. Patients who come to the clinic or are

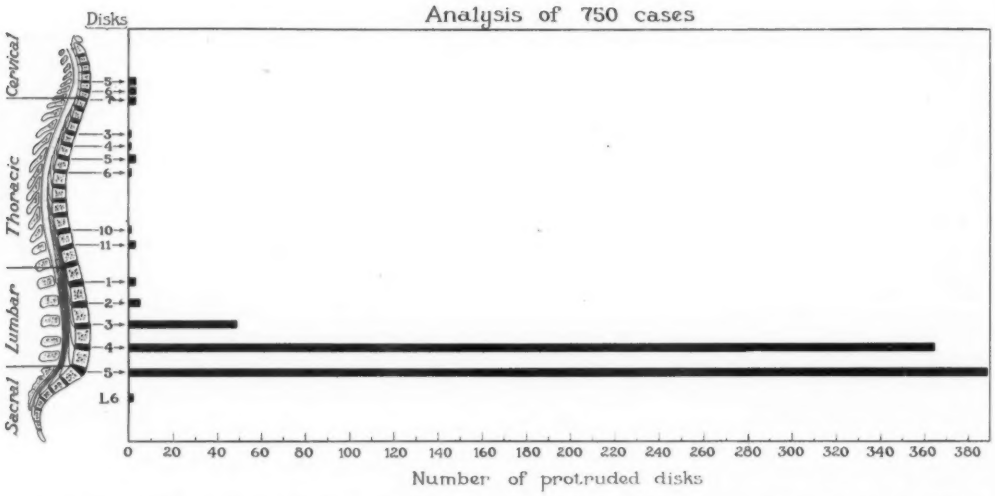

Fig. 1. Frequency of protrusion of different intervertebral disks into the spinal canal. On the left, a median section of the normal spinal column and, on the right, the interspaces and the numbers of protruded intervertebral disks which occurred in those interspaces. *L6* refers to the number of protruded intervertebral disks which were found in those cases in which there were 6 lumbar vertebrae.

referred here because of a complaint of backache or sciatic pain or both are usually those who have failed to obtain permanent relief by ordinary methods at home. The condition is most likely to be of long standing and since the syndrome of protruded intervertebral disk has become fairly well known many patients are referred for operation after the diagnosis of protrusion of a disk already has been made by the referring physician. These factors tend to make our statistics seem out of line with those of others.

According to Dr. Henderson, chief of the Section on Orthopedic Diagnosis, he and his associates in that section were called on, in 1940, to see approximately 5,500 patients who had backache as a symptom (including backache, sciatic pain, root pain, spondylitis, spondylolisthesis, sacroiliac disease, symptoms causing suspicion of a protruded disk, fibrositis, and so forth). It is from this group that our cases of protruded disk come. Approximately 13 per cent of the 5,500 patients were found to have one or more protruded disks as the cause of their complaints.

The incidence of protrusion of different disks into the spinal canal from their normal positions at the various levels of the vertebral column is shown in Figure 1.

DIAGNOSIS OF PROTRUDED INTERVERTEBRAL DISK

The diagnosis of a protruded intervertebral disk in the lumbar region of the spinal canal should not cause any difficulty when the patient presents the so called classic picture and gives the typical history. If a patient walks into the examining room with a listing of the body and appears to be suffering from pain, one is likely to find on examination (which should be made with the patient stripped) that there is a loss of the lumbar lordosis, that is, a flattening of the lower part of the back, marked spasm of the erector spinae muscles and limitation of the spinal movements. Hyperextension is likely to be not only limited but extremely painful. If the patient stands without a list he is prone to list on forward bending of the trunk on the pelvis with the knees stiff (straight). There usually is tenderness over the spinous processes of the lowest lumbar vertebrae. When the patient is examined while in the dorsal recumbent position, straight leg raising is limited and painful

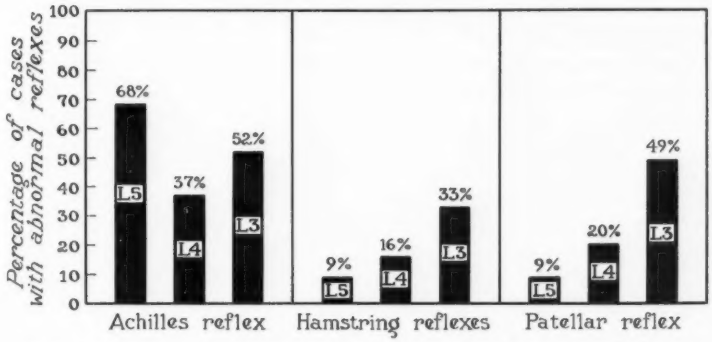

Fig. 2. Percentage of cases of protruded intervertebral disks in which the deep tendon reflexes in the lower extremities are abnormal. (From Craig, W. McK. and Walsh, M. N. *J. Bone Surg.*, 1941, 23: 417–434.)

on the side of the sciatic pain and in severe cases the straight leg raising test may give bilaterally positive results even though the patient has complained of pain in the course of only one sciatic nerve. Kernig's sign, likewise, will be positive and bending of the head forward on the chest will in some cases aggravate the low back or sciatic pain or both. The course of the sciatic nerve from the sciatic notch to the terminations of its terminal branches should be palpated to elicit the tenderness, which in some cases is extreme. Of course, while palpating, the examiner should seek to exclude a primary tumor of a nerve also. We have encountered one primary tumor of the sciatic nerve which masqueraded as a protruded disk.

The Achilles reflex on the side of the sciatic pain is usually diminished or absent. This is more likely to be true if the protrusion is lumbosacral than if it is at a higher level, but an absent Achilles reflex by no means excludes a protrusion at a higher level (Figs. 2 and 3). There may be slight disturbance of sensation over the outer and dorsal aspects of the foot, but extensive sensory loss is rare unless there is a very large lesion and then there are likely to be both motor and sensory loss and an associated disturbance of the anal and vesical sphincters.

The history of the patient presenting the foregoing findings in the typical case would be something like this: He or she is accustomed to heavy work which entails the placing of unusual stress or strain on the back. After some particularly unusual stress or strain there was an onset of backache which may have been associated immediately or subsequently with extension of pain along the course of one sciatic nerve, rarely both. The pain has been intermittent and on occasions has been relieved by rest, locally applied heat, diathermy, massage and other usual conservative measures. The pain has been aggravated by lifting, coughing, sneezing or straining at stool and has disturbed the patient's sleep. Often, loss of weight resulted due to loss of sleep and appetite.

With that history and those findings, protrusion of a lumbar intervertebral disk should be the diagnosis until proved otherwise. An unsuspected neoplasm of the spinal cord can duplicate the picture fairly well and the possi-

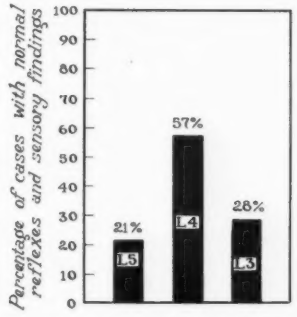

Fig. 3. Percentage of cases of protruded lumbar intervertebral disks in which the deep tendon reflexes in the lower extremities are normal.

bility of such a neoplasm must always be considered in the differential diagnosis along with the other conditions enumerated under incidence of protruded disks.

FINDINGS ON EXAMINATION OF SPINAL FLUID IN CASES OF PROTRUDED DISK

When the protrusion is large enough to produce gross neurologic findings as the result of extensive pressure on the spinal cord or cauda equina, the findings on lumbar puncture are likely to resemble those obtained in the presence of intraspinal neoplasms, namely, disturbance of the normal hydrodynamic relations with a tendency to subarachnoid block and a high concentration of total protein. However, since most of the protrusions encountered are relatively small and usually irritate and compress only one nerve root, the vast majority of the patients do not have a disturbance of the hydrodynamic relations of the cerebrospinal fluid, and the total protein content of the fluid is usually not markedly elevated. In approximately two-thirds of the cases the concentration of total protein in the cerebrospinal fluid is 40 milligrams per 100 cubic centimeters or more, whereas in fully a third the concentration of total protein is less than 40 milligrams per 100 cubic centimeters.

In the presence of low back and sciatic pain without a sensory level, if the fluid is yellow, if there is a high total protein content, or if there is a subarachnoid block, a neoplasm should be suspected. One of the commonest under these circumstances is an ependymoma which has arisen from the filum terminale.

CONTRAST MEDIA IN THE DIAGNOSIS AND LOCALIZATION OF PROTRUDED DISKS

Our early knowledge concerning the diagnosis and localization of protrusions of disks was obtained principally from the roentgenoscopic examination of the spinal canal into which radiopaque oil (lipiodol) had been injected. As our experience has increased, we have reached a point where we feel that our clinical diagnosis is just as accurate as the roentgenoscopic diagnosis obtained by the aid of radiopaque oil and more accurate than that obtained by the aid of air, which we now use almost routinely prior to operation.

Because of the slow absorbability of radiopaque oil and the medicolegal complications which might follow its employment, we have all but abandoned its use in cases of protruded disk. It is still used when indicated for the localization of intraspinal neoplasms and in selected cases of protruded disk.

Although air is absorbed rapidly and does not leave any telltale stigmas to be recorded on subsequent roentgen examination, its accuracy, according to Camp, is far less than that obtained with radiopaque oil.

One should not expect the roentgenologist to be able to diagnose and localize protruded disks in a very high percentage of cases with air or oxygen. Spinograms (air "myelograms"), when considered as only a part of the examination and evaluated along with the history and other findings, are of definite value, but alone they are often valueless. One of the most important uses for air in this group of cases is to exclude an unsuspected intraspinal neoplasm and the presence of multiple lesions. Air in our experience is practically valueless in thoracic and cervical intraspinal lesions. Its use in our hands is restricted almost entirely to those cases in which a lesion in the lumbar portion of the spinal canal is suspected.

The technique we employ in dealing with patients suspected of having a protrusion of a lumbar disk is as follows: The patient is given a sedative, usually one of the barbiturates, about 30 to 45 minutes before being called to the x-ray room. He is placed on his right side on the tilting x-ray table while the table is horizontal. After the back has been cleansed with ether and alcohol, two coats of tincture of merthiolate are applied to the skin of the entire lumbar region. With the patient under local (1 per cent solution of procaine hydrochloride) anesthesia, a lumbar puncture needle is introduced into the subarachnoid space through the second lumbar interspace, that is, the space between the spinous processes of the second and third lumbar vertebrae. When fluid is obtained, a manometer (Ayer type) is connected and routinely the Queckenstedt test is performed. As has been stated, we do not expect to find a "block," for we are purposely puncturing above the site of the suspected lesion. After the pressures have been

recorded, 10 to 15 cubic centimeters of fluid is collected and placed in a sterile bottle to be sent to the cerebrospinal fluid laboratory for the following tests — Wassermann, globulin, cell count, total protein, and colloidal gold curve. Then the patient's head is lowered 40 degrees away from the horizontal by elevating the foot of the tilting x-ray table. All of the fluid in the lumbar portion of the spinal canal is then replaced with air or oxygen. Usually about 40 cubic centimeters of fluid, in addition to what was collected for a specimen, is obtained. We usually inject an additional 10 to 20 cubic centimeters of air but this should not be under undue pressure. Approximately 50 to 60 cubic centimeters of air is necessary to get a satisfactory filling of the lumbar subarachnoid space.

While the head is still low and after the lumbar puncture needle has been removed and the puncture wound has been sealed with sterile cotton soaked in collodion, stereoscopic lateral roentgenograms are made. Then the patient is turned over on his back and stereoscopic anteroposterior roentgenograms are made. The patient is then returned to his bed and is advised to keep his head low for 24 hours, during which time he receives inhalations of oxygen by mask in order to promote more rapid absorption of the air.

The interpretation of spinograms is very difficult and there are many pitfalls. One looks, however, not only in the anteroposterior but also in the lateral views for defects, due to a lateral or posterior deviation or both of the air shadow at one or more intervertebral spaces. As has been stated, the finding of a complete block is rare.

PREOPERATIVE PREPARATION

When it has been decided that a protruded intervertebral disk is present and operation is indicated, the latter should be carried out without delay. We have found from experience that it is better to delay the taking of roentgenograms of the spinal canal into which a contrast medium has been injected until the patient is ready to proceed with operation in case it is indicated. Even though air is used as a contrast medium, it is fairly common for the patients to experience considerable exacerbation of their low back and sciatic pain and in addition to complain of headache and of pain between the shoulders and around the chest after the introduction of air into the subarachnoid space. Likewise, the patient may be troubled with nausea and vomiting. Since the operative removal of a protruded intervertebral disk requires a relatively short period of hospitalization and since the reaction after the taking of spinograms may persist for several days, the economic factor alone is worth considering and the patient should be ready to go ahead with the operation in case it is necessary. Even in spite of a reaction after the taking of spinograms, we rarely find it needful to postpone the necessary operation. Usually the spinograms are taken in the morning and the operation is carried out the next morning, after the spinograms have been studied and interpreted in conjunction with the history and physical and neurologic findings and the results of the examination of the cerebrospinal fluid.

Elaborate preparation for operation is not required. The patient has had cleansing enemas preliminary to the taking of the spinogram and further attention to the bowel is not necessary. The patient is given a light supper on the evening prior to operation but breakfast is withheld on the morning of operation.

Commonly, if the patient is to have the usual anesthetic agent, namely, drop ether, 1/6 grain (0.01 gm.) of morphine and 1/150 grain (0.00043 gm.) of atropine are injected hypodermically approximately 30 minutes before administration of the anesthetic agent is started. If the operation is to be performed with the patient under spinal analgesia, 1½ to 3 grains (0.1 to 0.2 gm.) of pentobarbital sodium (nembutal) is administered 45 minutes to 1 hour before the spinal analgesic agent is to be administered, and 1/6 or 1/4 grain (0.01 or 0.016 gm.) of morphine, depending on the patient's age and weight, is given 30 minutes prior to the introduction of the spinal puncture needle. The same preoperative medication plus atropine is used if the patient is to be operated on under the influence of pentothal sodium which is intravenously administered.

CHOICE OF ANESTHETIC AGENT

As was stated previously, the anesthetic agent most commonly employed is drop ether. The patient is anesthetized by a combination of nitrous oxide and oxygen, and then drop ether is substituted. Some of the surgeons at the clinic prefer to have a McGill intratracheal tube introduced after the patient is asleep and then drop ether is administered over the outer end of the intratracheal tube. If the patient has recovered recently from an infection of the upper part of the respiratory tract or there is any question regarding the advisability of using an inhalation anesthetic agent, such as ether, the operation may be performed while he is under spinal analgesia or under the influence of intravenously administered pentothal sodium. The latter anesthetic agent is particularly useful for persons who are unduly nervous, for those who have severe hypertension, and for those who have asthma or hay fever

OPERATION

After the patient has been anesthetized he is placed on the operating table in the face down or prone position except in cervical operations, in which we prefer to operate with the patient in the upright position, such as is used for operations in the posterior fossa of the skull. The skin about the region of the operation should be shaved carefully and cleansed thoroughly with ether and alcohol before the cutaneous antiseptic agent is applied. The cutaneous antiseptic agent which we use is tincture of merthiolate. Two liberal coats of the antiseptic agent are applied. Double towels are then placed to either side of the spinous processes and about 1½ inches (4 cm.) lateral to the midline. Double towels are then placed above and below, crossing the towels previously placed and only far enough apart to leave uncovered an area of skin sufficient for adequate exposure. Ordinarily, this interval should not exceed a distance corresponding to three spinous processes.

The incision is midline and is carried down to the tips of the spinous processes. Ordinarily, in case of unilateral symptoms and signs it is necessary to reflect the muscles only on one side. If the symptoms and signs are bilateral or if a midline protrusion of the disk is suspected the muscles should be reflected bilaterally. The muscles are reflected from the spinous processes and laminae by means of a sharp chisel and the reflections should be subperiosteal. In this way hemorrhage from the muscles is reduced to a minimum. When the muscles have been reflected, gauze sponges are packed between the bone and the muscle while the previously caught bleeding vessels in the skin and subcutaneous tissue are controlled by electrocoagulation applied to the hemostatic forceps. Care should be taken in electrocoagulating these vessels lest too much heat be applied with the resultant sloughing of the cutaneous margins. The gauze packed between the bone and the muscle serves two distinct purposes. It further tends to control whatever slight bleeding may be occurring, either in the bone or in the muscles, and it tends to iron out the muscles and provide better exposure. If the muscles are reflected over a distance sufficient to permit the introduction and use of the large laminectomy self-retaining retractors, these are inserted deeply into the wound and the muscles are spread away from the bone. If the incision is short, like that now ordinarily employed when the protruded disk is to be removed without the sacrifice of any bone, the medium-sized self-retaining retractor is used to spread the skin and the gauze sponges are left packed in the wound until the wound towels have been applied.

If the procedure usually employed by one of us (Love, 8) is used, the ligamentum flavum at the interspace where the protruded disk is located is resected by the aid of a ground-down Adson curved periosteal elevator. The ligament is cut away from the upper margin of the lamina of the vertebra below and then the periosteal elevator is inserted under the lower margin of the lamina of the vertebra above. The ligament is dissected free above and below, down to the dura mater, seized with a Kocher forceps, cut away from the interspinous ligament with a pair of scissors, and then turned laterally and resected with scissors as far laterally as possible. While carrying out this procedure, one usually notices that the ligament is thicker, less yellow and more whitish or grayish and much more fibrous than is the normal ligamentum flavum. Underneath

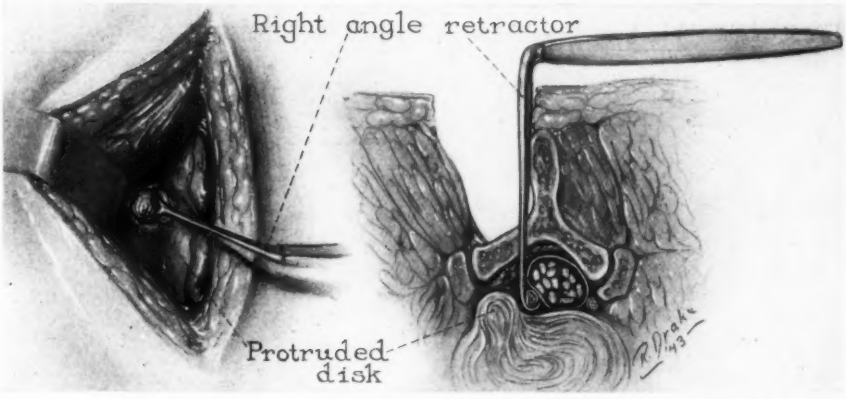

Fig. 4. Extent of the operative procedure which is required in the average case of protruded intervertebral disk. A special right-angled retractor is in place, retracting the edematous compressed nerve root and exposing the protruded disk which is to be removed with a modification of the Gruenwald forceps.

the ligament one encounters usually either a large, tortuous extradural vessel or an enlarged, hyperirritable nerve root. Underneath the nerve root the protruded disk is palpated. If the protrusion is the typical unilateral extrusion the nerve root is retracted toward the midline with the straight or right-angled (Love, 7) nerve root retractor (Fig. 4). At this point the surgeon will find in many cases that the protrusion is lying free and can be lifted out with the Gruenwald ethmoid forceps, or he may find that the protrusion is still covered by the posterior longitudinal ligament. Often this ligament is so thin and yielding that it is penetrated easily with the use of a forceps. Sometimes the ligament is dense and incision with a sharp instrument, such as the ureteral knife, is required before the protrusion can be removed. The protruded fragments of cartilage are then removed with the Gruenwald forceps. Care should be exercised lest loose fragments within the center of the disk be overlooked. In the majority of cases, the protruded portion of the disk can be removed in this fashion without opening the dura mater and without the sacrifice of any bone.

If there is unusual narrowing of the interlaminar space, if the protruded fragment of cartilage has wandered away from its usual position opposite the interspace or if the protrusion is unusually large or is in the midline position, it may be necessary to do some type of laminectomy. Classic laminectomy, consisting of the removal of one or more spinous processes and two or more laminae, may be required. In this operation, as in all operations, adequate exposure is essential. The articular facets should always be preserved. It may be sufficient to shear off a portion of the spinous processes of two adjoining vertebrae with or without the removal of the margins of the laminae of the adjoining vertebrae. Hemilaminectomy without the sacrifice of a spinous process may afford ample exposure. At times one need only remove a few bits of bone from the lower margin of the lamina of the vertebra above the interspace or from the upper margin of the lamina of the vertebra below the interspace at which the protrusion has occurred.

Rarely, when an unusually large midline protrusion, because of its size, has produced paraplegia and considerable edema of the cauda equina, it may be necessary to approach the protrusion transdurally. In such cases it is essential to perform laminectomy and to incise the dura mater, first posteriorly, and then anteriorly over the dome of the protrusion between the strands of the cauda equina. Under such circumstances, the cauda equina should be protected carefully with strips of cottonoid

soaked in physiologic saline solution, and manipulation of it should be kept at a minimum. Ordinarily, it is unnecessary to suture the anterior incision in the dura mater unless one has had to make an unusually long incision or sharp bleeding has been encountered anterior to the dura mater. The posterior incision of the dura mater should always be closed to prevent a cerebrospinal fluid leak and in order to maintain the hydrodynamic effect of the cerebrospinal fluid and thus minimize the danger of postoperative hemorrhage.

Previously, one of us (Love) and Camp (9) stated that drainage of the wound usually is necessary. As our experience with this lesion has increased we find that it is rarely necessary now to insert a drain in the wound. There are two principal reasons why this is so: (1) The removal of bone has been reduced to a minimum. (2) The dura mater rarely is opened. Since the dura mater is not opened, the normal hydrodynamic effect of the cerebrospinal fluid is maintained and, even though bleeding is sharp during the retraction of the nerve root for the removal of the protruded portion of the disk, as soon as the retraction is stopped the thin walled extradural veins cease to bleed. If bleeding should continue, the application, over the site of bleeding, of a small pledget of muscle which has been pounded thoroughly to liberate the tissue juices will suffice to control hemorrhage. If, in spite of this, bleeding should continue, a strip of plain gauze 1 inch (2.5 cm.) wide should be plicated over the site of the bleeding and then suction applied to a strip of cottonoid placed on top of the plicated gauze. As soon as the bleeding has been controlled, the cottonoid should be removed before the wound is closed. The strip of gauze should be removed at the end of 48 to 72 hours. If the strip of gauze is packed against the nerve root or anterior to the common dural sac, pentothal sodium should be administered intravenously and the patient should be asleep before it is removed. Otherwise, excruciating pain will result when traction is applied to the gauze.

Whether or not the wound is drained, it should be closed in layers. The muscles are approximated with interrupted No. 1 chromic catgut sutures, as is also the fascia. The subcutaneous tissues should be anchored to the fascia with No. 0 chromic catgut in order to obliterate the dead space and the skin should be approximated with a continuous stitch of silk. Either sponges of dry gauze or sponges soaked in alcohol are applied to the wound and then a large cotton pad dressing is applied over the gauze and fastened securely with adhesive tape. The dressing is not sealed in with the adhesive tape, as it is considered advisable to permit air to get to the wound and surrounding skin. In this way the likelihood of maceration of the skin, particularly if there is drainage, is minimized.

POSTOPERATIVE CARE

Patients who have had an operation on the back for the removal of a protruded intervertebral disk are placed on their sides in a bed that has boards under the mattress, and they are en ouraged to turn themselves as soon as they feel like it and as often as they desire, although they are advised to refrain from lying on their backs until the wound is well healed. The reason for avoiding the supine position is the feeling that the other positions are more comfortable and the wound will heal better if pressure is not permitted. During the first 24 to 48 hours an order is left for the patient to have 1/6 grain (0.01 gm.) of morphine every 4th hour if it is needed. Many of the patients do not require the morphine. Patients are allowed to take fluids as soon as they have the desire and by the 2d or 3d day they can be on a full hospital diet. If the patient is unable to void, women are catheterized every 8th hour beginning the morning after the day of operation. At this time men who have had one of the less extensive operations are permitted to stand beside the bed and use the urinal and if they are unsuccessful they too are catheterized. It is unusual for a patient to need catheterization after the 2d or 3d day. The bowels are opened on the morning of the 3d day with the assistance of an enema of soapsuds.[1] The patients who have had the less extensive operations are permitted to dangle their feet over the side of the bed on the 5th postoperative day, to sit in a chair on

[1]More recently the patients sit up the 4th day, have castor oil that night and go to the bathroom the next morning.

the 6th and to begin walking on the 7th. The sutures in the skin are removed on the 9th or 10th day after operation.

Most of the patients are out of the hospital by the 12th day after operation. After leaving the hospital, the patients report to the office for postoperative examination and advice before dismissal from our care, which usually takes place about the 14th or 15th day after operation. All patients are advised to spend 3 months convalescing before returning to their former activities. Those in the heavy types of work need a period of reconditioning or training before assuming full duties.

COMPLICATIONS

Although patients suffering from protruded intervertebral disks come to the physician seeking relief principally from pain, which may vary tremendously in intensity from a minor annoyance to that which is so severe as to result in complete disability, a protruded disk may give rise to complications which threaten the life of the patient. Some patients, because of the severity of the pain, lose their appetites and are unable to sleep. As a result of these two factors the patient may lose considerable weight and become debilitated, or he may become addicted to the use of narcotic agents. If the protruded portion of the disk is not removed and pressure on the spinal cord or one or more nerve roots is allowed to persist, irreparable damage to the nervous system may occur. Marked atrophy of the muscles of an extremity may take place, drop foot may develop, or if the protrusion is large, paraplegia, in the case of a lumbar lesion, or even quadriplegia, in the case of the less common cervical lesions, with loss of control of bowel and bladder, may occur. As a result of the disturbance of function of the bowel and of the urinary tract, severe renal damage, uremia, and death may ensue.

Probably under the head of complications one should include the discussion of other conditions which might be present and might influence the diagnosis, the treatment, and the result of the treatment obtained in cases of protruded intervertebral disk. Although we have been taught, and ordinarily try, to make one diagnosis explain the symptoms of a given patient, it may be necessary in some cases to make multiple diagnoses. For instance, it is fairly common for a patient who has a protruded disk to have definite evidence also of arthritis of the spine. Then, too, occasionally one sees a patient suffering from diabetes mellitus who has the symptoms and signs of a protruded intervertebral disk. MacKay has reported from the service of one of us (Love) the association of protruded intervertebral disk and Paget's disease of the pelvic bones. In the presence of one of these complications one cannot anticipate complete relief of all the patient's symptoms even though one operates and removes a protruded intervertebral disk. However, provided the patient and the surgeon discuss the situation and the patient understands that there are two or more factors which may be playing a part in the production of the symptoms from which he seeks relief, it is our feeling that, if a protruded intervertebral disk is present and is contributing to the production or aggravation of the patient's symptoms, in view of the small risk of the operative removal of such a protruded disk operative removal should be advised and carried out.

FUSION

The advisability of performing a bone graft at the time of removal of a protruded intervertebral disk is debatable. There are those who believe that in every case it would be advisable to insert a bone graft after the removal of a protruded intervertebral disk. At the other extreme are those who believe that a bone graft is rarely, if ever, necessary. Obviously, the truth lies somewhere between these two extremes of opinion. It is our feeling that in some cases a bone graft not only is indicated but is necessary if the patient is to obtain the best result from his treatment. In cases of frank spondylolisthesis in which there is an associated protrusion of an intervertebral disk and particularly if the lesion is at the lumbosacral interspace, we feel that a bone graft should be performed. For patients who narrate a long history of static backache before the onset of sciatic pain and whose roentgenograms reveal definite evidence of disease of the vertebrae, fusion will, we believe, give the best result. Narrowing of an interspace

per se is not a sufficient indication for fusion. Neither is the presence of spina bifida occulta.

If a fusion operation is to be carried out, we at the clinic work with the consultants in the orthopedic section at the time of the operation. While the neurosurgeon is removing the protruded intervertebral disk, the orthopedic surgeon removes a massive bone graft from the flat internal surface of the tibia. When the neurosurgeon has completed his part of the operation, the orthopedic surgeon takes over and inserts the bone graft to accomplish the desired fusion. Although, when two surgical teams operate together, the actual time required for the operation is not increased appreciably, the period of hospitalization and time of convalescence are prolonged considerably. This is a factor which we feel should be considered carefully before one advises such a procedure. For instance, even though the indications are present for a combined operation, if the patient has reached the age of 55 years or more, prolonged hospitalization may increase the risk. A patient who has reached this age may be able to avoid the things which ordinarily produce backache and to get along quite satisfactorily without the fusion being performed.

RESULTS

The results of the operative removal of protruded intervertebral disks have in our hands been excellent. The mortality rate has been less than 0.25 per cent. Complete relief of the symptoms for which the operation is performed should occur in 80 per cent of cases. The patients who have not sustained irreparable damage to the spinal cord or nerve roots should obtain relief without any sequelae. In cases in which considerable atrophy of the muscles of an extremity has developed or in which there is extensive and severe sensory loss, or drop foot, the patients may be relieved of the pain of the nerve root for which the operation is performed but the gross neurologic changes may persist. The results in operations for protrusions in the lumbar region of the spinal column are consistently better than those obtained in operations for protrusions in the cervical and thoracic portions of the spinal column. There has been an incidence of approximately 2 per cent of recurrence of the protruded disk in the cases in which protrusion was in the lumbar region. The recurrence in practically every case has been at the site of the original protrusion and the operative treatment consists in removal of the recurrent protruded fragment of cartilage which is compressing the nerve root. A small group of patients, although relieved of their sciatic pain, will continue to complain of aches and pains in the lower part of the lumbar region which may vary in intensity from a mild nuisance to incapacity for the heavier types of work.

In order to achieve what we consider to be satisfactory results in the treatment of intractable root pain due to protruded intervertebral disks, every case in which a protrusion of an intervertebral disk is suspected is evaluated very carefully by our staff and all such patients are seen in neurosurgical consultation before a diagnostic lumbar puncture is performed. In this way many borderline patients, many who can carry on quite satisfactorily with conservative orthopedic measures, and many who have symptoms and signs suggesting, but not definitely indicating, protruded intervertebral disks, are spared the discomfort, time, and expense of lumbar puncture and visualization of the lumbar portion of the spinal canal. The conservative orthopedic measures which are advised by our orthopedic colleagues consist of the wearing of a so called sacroiliac belt by patients suffering from a low back or sciatic pain or both. In addition, physical therapy in the form of heat and massage is prescribed if the patient is ambulatory. If the patient is suffering so that he is unable to be up and around, rest in bed with boards under the mattress, bilateral Buck's extension, and a lumbar sling are prescribed. In addition he may receive diathermy treatments and physical therapy. Many patients suffering from protruded disks will tolerate such treatment poorly and neurologic signs may even develop which will give unmistakable evidence of an intraspinal lesion and thus give clear indication for operative intervention. Many borderline patients when first seen are advised to follow conservative nonoperative treatment for 3 to 6 months before considering intraspinal surgical treatment.

Since the operation for the removal of a protruded intervertebral disk is a highly technical surgical procedure and one which not only can produce a brilliant result but also can result, if improperly conceived and carried out, in complications which are more disastrous than the original condition for which the procedure was designed, it is essential that as much as possible be known about the nature and location of the intraspinal lesion before the operation is undertaken. A carefully conceived and well executed removal of the offending cartilage should result in the alleviation of the patient's pain and disability with a minimal risk to life and limb. The mortality rate at the clinic has been less than 0.25 per cent, as previously stated.

The results of operation on patients who are receiving compensation or insurance and on those who have litigation pending have not been so good as the results for the patients who are interested only in getting well. This, it would seem, is natural and easily understood. On the other hand, it does not mean that patients in whose case there is a medicolegal angle do not obtain relief or do not return to their former occupations, nor is it intended as justification for withholding necessary surgical treatment from patients who are found to fall into this group. However, one must realize that medicolegal cases do present a real problem and that it is necessary not only to find the cause of the patient's disability and to remove it but also to convince him that he has been relieved and that he is able to return to his work.

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A COAGULUM CONTACT METHOD OF SKIN GRAFTING AS APPLIED TO HUMAN GRAFTS

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DURING the last 2 years a new method of skin grafting was developed and the preliminary animal experiments were reported (1). While further simplifications have since been made in the technique (2), the method as first propounded has been applied to human grafts and is the basis of this report.

METHOD

Into a 10 cubic centimeter syringe containing 1 milligram of heparin[1] dissolved in 1.0 cubic centimeter of Tyrode's solution (a buffered salt solution), 5 cubic centimeters of the patient's blood are drawn. The blood is centrifuged and the plasma transferred to a small 5 cubic centimeter test tube, all procedures being done under sterile conditions. One and a half cubic centimeters of Tyrode's solution are added to the remaining red cells and buffy coat (white cells) or to the buffy coat alone if it is convenient to separate it from the erythrocytes. This cell mixture is agitated vigorously, and to assure thorough disintegration of the cells a few sterile glass beads are added. If the buffy coat has not been separated from the red cells the mixture must be centrifuged and the supernatant fluid removed to another sterile tube. If the buffy coat alone is used, centrifugation is not necessary as the cellular fragments do not interfere with the grafting. This fluid, whether prepared from the buffy coat or from the erythrocytes plus the buffy coat will be referred to as "cell extract."

In preparation for the actual grafting the recipient area is washed with warm sterile saline and dried with gauze. The donor area is sterilized by whatever method the operator prefers. Thin split grafts to full thickness grafts can be used, the size of the graft being of any desired dimensions. The graft is turned upside down on a sterile piece of gauze, without washing in saline as such washing tends to remove tissue extracts which aid in producing the required coagulum. With a camel's hair brush the under side of the graft is moistened lightly with the cell extract. With another brush the plasma is painted on the recipient area. The graft is quickly fitted into the recipient area. The edges are carefully adjusted and slight pressure with the forceps is applied to the graft to assure good contact. It adheres within a few minutes. A single strip of boric acid gauze is lightly placed over the graft to protect it from infection and drying. No other dressings are applied; no stitches are needed. If esthetic results are desired, the graft is made slightly larger than the recipient area and the edges are trimmed to fit exactly. Even the edges will adhere well if there is no bleeding, and bleeding rarely occurs as no stitches are required to fix the graft in place. Within 48 hours the graft becomes purplish and the circulation sufficient to take care of any serous fluids which might accumulate underneath. Sections of grafts on rats have shown that the small vessels are filled with healthy erythrocytes. In fact it is difficult after more than 48 hours to determine microscopically the exact site of union between the graft and underlying tissue.

Through the co-operation of the department of surgery of Temple University Hospital we have been able to apply numerous grafts on 10 different patients. Approximately 100 square inches of skin have been grafted of which less than 1 square inch has been lost. The varying clinical problems and the wide range in the type of grafts used have been so inclusive that they give a good idea of the scope and reliability of this new method. I am especially indebted to Dr. W. E. Burnett through whose co-operation we were first able to use the method clinically and to whom the first 5

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[1] One milligram heparin (Hynson, Wescott and Dunning) prevents the coagulation of 7.5 c.c. cat's blood for 24 hours.

cases of this series belong. The cases in this series have been reported chronologically and the surgeon in charge in each instance indicated. I should like to take this opportunity to express to them my appreciation for their co-operation and for their permission to publish the brief abstracts of their patients' histories.

CASE HISTORIES

Case. 1. A white boy, aged 5 years, had the tip of his nose bitten off by a dog on September 14, 1942. He was treated with sulfathiazole ointment (dog showed no evidence of hydrophobia). A thick split skin graft was applied on September 15, 1942. The graft turned deep purple about 48 hours later. The patient went home without a dressing 3 days later. For end-results see Figure 1. (Dr. W. E. Burnett's case.)

Fig. 1. Case 1. Three weeks after grafting.

Case 2. A colored mentally backward child, aged 19 months, had the left arm burned 6 months previously with resultant disfigurement and scarring, over left wrist, left forearm, and elbow, causing much deformity. The scar was removed and a thin split graft was applied over left wrist and left elbow. The scar of left forearm was removed and the wound was closed with wire sutures. Three days later, viridans streptococci infection developed in forearm and at edges of graft. The graft was well vascularized and there was no loss of skin notwithstanding infection. Sulfathiazole ointment was applied. (Dr. W. E. Burnett's case.)

Case 3. White male, aged 28 years, received a crushed index and middle finger on October 11, 1942. Débridement was carried out and a medium split skin graft was applied on index finger by means of the new method. Stitches and pressure dressings were applied on middle finger. Patient traumatized index finger during the night with much resultant bleeding. Neither graft took and viridans streptococci were isolated from underneath the graft. The underlying tissue was craggy and not firm. (Dr. W. E. Burnett's case.)

Case 4. White female, aged 49 years, was treated with x-ray elsewhere for hypertrichosis of skin. Patient developed epithelioma. This was removed and left to heal completely. The scar was then removed and a full thickness graft was applied immediately. The underlying tissue was fibrous. There were several vessels which bled freely and were tied with silk sutures. Vascularization was established within 48 hours (Figs. 2 and 3). (Dr. W. E. Burnett's case.)

Case 5. White male, aged 45 years, had his left thumb partially crushed. Amputation was advised at another hospital and the tip of the phalanx was amputated. Débridement to the bone was carried out on the medial side February 9, 1943. Due to infection the grafting was postponed. On February 25, 1943, there was still a mixed coliform bacillus and Staphylococcus albus infection. A thin split graft was applied. It became deep purple within 48 hours. Patient returned to work 2 weeks later. (Dr. W. E. Burnett's case.)

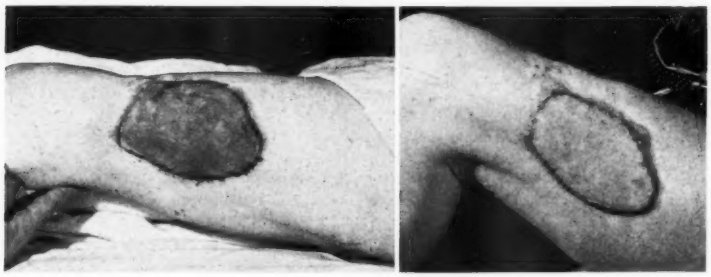
Case 6. White female, aged 71 years, had a squamous cell carcinoma, grade III of the left thigh removed on March 1, 1943. Some Staphylococcus albus infection of the edges developed. Full thickness graft (4 mm.) measuring 8.5 by 9 centimeters was removed from under the right breast where there was excessive skin. A few streaks of yellow fat were adherent to the under surface. Graft turned deep purple within 39 hours. As the graft was too large and too thick at the edges for the area it was trimmed down after 10 days and the edges were sewed down. The graft edges when trimmed down bled freely and a section was taken to determine its appearance (Figs. 4 and 5). (Dr. J. Blady's case.)

Case 7. Colored boy, 5 years of age, was scalded with hot water on the right arm, elbow, and shoulder. He was sent to Municipal Hospital with scarlet fever. Several thin split grafts and one full thickness graft were applied on the elbow. They were deeply colored within 48 hours. During the grafting of numerous pieces 1 graft was inadvertently brushed off and dried with the clot on. It was replaced, but only a small fragment of this took. All the other 6 grafts took well. (Dr. R. Teehan's case.)

Case 8. Female, aged 54 years, with chronic mastoiditis was operated on and a full thickness skin graft was applied. There was much bleeding at the time of fixation but the result 3 weeks later appears to be satisfactory. (Dr. M. S. Ersner's case.)

Case 9. Colored male, 48 years of age, burned his right leg in boiling alkali solution. On January 23, 1943, débridement was carried out. He was seen on April 15, 1943 and skin grafting over approximately 40 square inches was done on April 16, 1943. Thin and thick split skin grafts were used. Granulation tissue had been trimmed 1 week previously. Three days later suppuration occurred around the grafts and granulation tissue. Mixed hemolytic Staphylo-

Figs. 2 and 3. Case 4. Left, 48 hours after grafting; right, 5 days after grafting.



Figs. 4 and 5. Case 6. Left, 48 hours after grafting; right, 3 weeks after grafting.

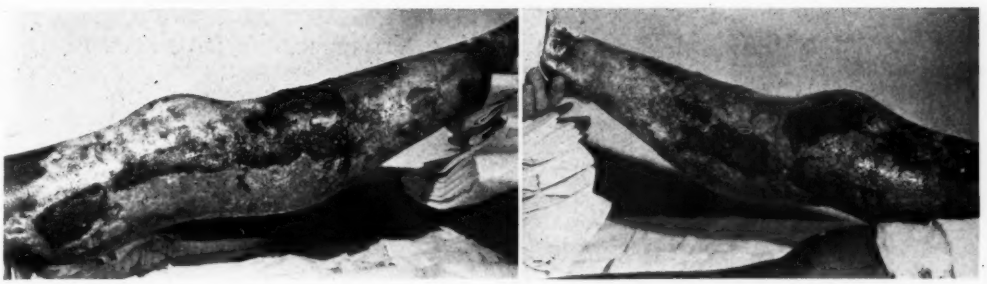
coccus aureus (pathogenic strain), hemolytic streptococcus, Group A and Staphylococcus albus were isolated. This infection was kept under control by sulfathiazole spray. On April 26, 1943, the grafts were already beginning to grow out from their edges. There was no loss of tissue. More grafts were fixed in the remaining denuded areas. These were well fixed and grew as did the previous ones (Figs. 6, 7, 8, 9). Each grafting took about one-half hour. (Dr. G. P. Giambalvo's case.)

Case 10. White woman, aged 67 years, had an epithelioma of the scalp removed on April 22, 1943. It was left to granulate in but on April 26, 1943, no granulation tissue had appeared. No infection was present. Grafting was carried out on April 26, 1943. Thick and thin split grafts both were used. Grafts turned purplish though not as intensely as usual within 48 hours. The result was satisfactory. No loss of graft occurred (Dr. J. N. Coomb's case.)

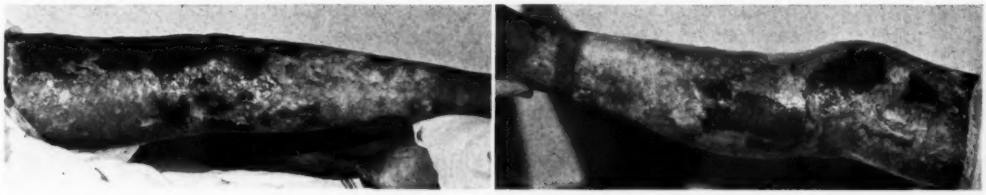
EVALUATION OF METHOD

The method has the advantage of not requiring compressive dressings which not infrequently interfere with the fixation of the graft and are difficult to apply in certain areas of the body. No stitches are used and thus no fresh or additional points of bleeding are created. Likewise no stitch scars result. Furthermore, the coagulum formed when the cell extract and the plasma come into contact with one another not only fixes the graft in place but gives the cells an ideal medium to grow in. This is the same type of medium used *in vitro* in tissue culture except that the plasma and cell extract here are autogenous. The rapid growth is further enhanced by the extract from the buffy coat (leucocytic cream) which seems to have a greater stimulus to cell growth than splenic tissue extract which is frequently used in tissue culture. All solutions and media being buffered the ideal conditions for cell growth are completely realized. The coagulum helps to prevent too much exudation and, if there is any, the rapid re-establishment of the circulation takes care of this by absorption. On the 4th day the skin desquamates as if it had been sunburned but otherwise retains a normal appearance. With split skin grafts and healthy granulation tissue the edges of the graft will be seen to proliferate independently by the 10th day.

The success of the graft can be determined within 48 hours, though when it is colored skin it is more difficult to determine for the uninitiated. If the surface of the underlying granulation tissue is unusually irregular the graft appears to smooth it out very much like



Figs. 6 and 7. Case 9. Left, External surface of right leg; right, medial aspect of leg, both 48 hours after grafting.



Figs. 8 and 9. Case 9. Left, External surface and posterior surface of right leg; right, medial aspect of same leg, both 48 hours after second grafting and 10 days after first. Patient ambulatory and discharged 19 days after first grafting.

normal skin would do and the trimming of granulation tissue does not have to be quite as extensive as for other grafts. Thick skin grafts take on a deep purplish hue regularly within 48 hours, and sometimes, as in Case 6, within 38 hours. It is not essential to have granulation tissue as shown by Cases 4, 8, and 9. If the edges of the graft can be well fitted with adjacent skin as in Case 1, the rapid growth results in a very satisfactory cosmetic effect with scarcely more than linear scarring. The method has the advantage of technical rapidity, as it does not require stitching; thus time is saved for the surgeon. Fixation of the graft within 4 days permits the patient to be discharged and merely return to the clinic for observation for the next few days; thus hospital expense is saved for the individual and bed space for the hospital.

As serum does not accumulate underneath the graft, grafts are not lost because of such "floating," and no incisions need be made even in the largest grafts (15.0 by 12.5 cm.) to allow for exudation. One full thickness graft (Case 6) had some fat adherent to it. Thus, in certain cases it is hoped that tube grafts and pedicle grafts will be dispensed with, and thus again the patient will be saved long hospitalization and weeks of inactivity. To what extent this method will replace other methods of grafting, the future only can tell but experience has shown that its use is greater than was anticipated when it was first developed. Besides, the method in itself opens new fields of application which are now being developed with the co-operation of the surgical department.

SUMMARY

A discussion of the technique, use, and application of the new coagulum contact method of skin grafting with a report of the results obtained in 10 clinical cases is presented. A description of further simplifications of the method using dried plasma and leucocytic cream as successfully employed experimentally in animals has been reported elsewhere.

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UMBILICAL HERNIA IN THE BAD RISK PATIENT

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THE value of herniotomy for the relief of umbilical hernia has been overlooked in recent years. This paper will attempt to demonstrate its usefulness as a means of reducing the needlessly high mortality in old, obese, bad risk patients with large, often strangulated hernias, and the operation will be endorsed as the surgical method of choice in all bad risk cases. A series of 39 consecutive cases of operation for umbilical hernia in patients 60 years of age and older will be analyzed. For purposes of comparison, the successful results of herniotomy in 2 private patients of 70 will be described.

The scant attention paid to herniotomy in the recent literature appears to be due to an emphasis on the avoidance of sepsis and recurrence, and an underemphasis on the reduction of operative mortality. Surgeons have concentrated their attention on the technical details of operation, on the choice of methods of repair and of suture materials, and the selection of the proper anesthetic, with probable failure to realize that in the majority of these cases incision is better than repair, herniotomy better than herniorraphy.

The operation of cutting the constricting ring to relieve strangulation made its appearance in the 16th century. In 1881, Lucas-Championnière repaired umbilical hernia by overlapping the lateral edges of the rectus fascia, and 18 years later Mayo suggested transverse overlapping. In 1908, Hahn advocated a two stage operation, in which between the stages binders applied increasing extra-abdominal pressure to regain the lost "right of domicile"; following weight reduction and general physical improvement, the defect was repaired. In 1916, Simmons analyzed 70 consecutive cases and concluded that recurrence in adults could be reduced from 50 to 10 per cent by employing the Mayo method. In 1940, Mahorner demonstrated that the incidence of wound infection could be decreased from 20 to 10 per cent by the use of silk sutures. In 1942, Taubenschlag, advocating the use of cotton thread, observed that in some cases lipectomy is necessary as a preparatory operation along with weight reduction to prevent recurrence.

The management of bad risk patients has received more attention in surgical textbooks and treatises. Bickham points out that operation should be undertaken either for relief of strangulation or for radical cure, intimating that ordinarily it should not be performed for both. Cutler and Zollinger state that all umbilical hernias in adults should be repaired if the patient's condition permits—a proviso that is too frequently disregarded. Psychologically it is difficult for a surgeon to stop short of repairing a hernia, let alone making it larger. Babcock maintains definitely that in large, strangulated umbilical hernias the constriction should be relieved by incising the ring of the sac, thus converting it and the abdominal cavity into one large space; later, after suitable reduction and preparatory treatment, hernioplasty may be done. If the bowel is gangrenous, Babcock recommends bringing the loop out through the incision, as in the first step of a Mikulicz colostomy resection. Homans concurs by suggesting release of the ring—and often of the strangulating band within the sac—under a local anesthetic.

In September, 1942, I was confronted in my private practice with 2 cases of strangulated umbilical hernia in septuagenary, bad risk patients; these are reported herein. Both patients were treated conservatively by herniotomy under local anesthesia. The results were so gratifying that they led to the investigation of a series of 39 such cases in which patients were operated on for umbilical hernias at the Boston City Hospital between 1932 and 1942. A great many more patients than this were admitted to the wards with this diagnosis, but for various reasons the patients did not undergo surgery. In some cases the diagnosis of hernia was incidental; in others the hernia reduced spontaneously or was reduced by taxis, but recurrence neces-

sitated several readmissions. Many patients were considered to be too poor risks for operation, and a few were admitted moribund. This study was limited to patients of 60 years of age and older who were operated on, since apparently the greatest improvement in treatment is to be found in this group.

The sex distribution was 31 women and 8 men, a ratio of 4:1, agreeing with that of most published series (4). On the whole, the women had larger hernias than did the men, only 2 of the latter having large defects. This observation, accompanied by the fact that most of the patients were markedly obese, corroborates the accepted theory that obesity and repeated pregnancies are the common etiological factors leading to umbilical hernia in adults.

The ages ranged from 60 to 88, with an average of 68. Twenty-four patients were in their sixties, 13 in their seventies, and 2 in their eighties. This diminishing incidence is a natural expectation with declining years. The age factor had considerable prognostic bearing within the series, the mortality rate being 2.5 times greater in the 8th and 9th decades than in the 7th.

In all the patients, whether the hernia was uncomplicated or strangulated, and regardless of other surgical procedures, repair was attempted. Twenty-six of the 39 operations were performed by members of the visiting staff, 8 by members of the resident staff, and 5 good risk cases by the house officers under supervision. The length of operation varied from 18 minutes to 2 hours and 38 minutes. The method of repair usually adopted was the Mayo procedure with "vest over pants" transverse overlapping.

The mortality rate was enlightening. Homans gives an overall rate of about 30 per cent, even when the patients are in skillful hands. Wangensteen emphasizes that strangulating obstructions and late cases of simple obstruction with great distention contribute largely to the mortality. In the present series 26 patients recovered and 13 died, a gross mortality of 33 per cent. Sixteen patients were operated on electively, with 2 deaths, or 12 per cent; of the remaining 23 handled as emergencies, 11 died, or 48 per cent. The method and length of operation, rather than skill, technique, or type of anesthesia, probably account for these disappointing figures.

The fatal cases presented a fairly constant picture. The patients were distinctly old, obese, and dyspneic. Hypertension, arteriosclerotic heart disease, fibrillation or decompensation, and chronic nephritis appeared time and again among the final diagnoses. The hernias were huge and gave rise to acute predicaments after being present for an average of 15 years. After 2 or 3 days of obstruction and acute illness, these patients entered the hospital, where immediate operation was performed. Usually either local or spinal anesthesia was employed, supplemented if necessary by nitrous oxide, ether, or cyclopropane and oxygen. The operations were tedious and disappointing. The immediate complications were surgical shock and atelectasis. There were 5 cases of major wound sepsis, 2 of peritonitis, and 1 each of septicemia and pulmonary infarct. Most of the cases, however, followed the same pattern: operation, cardiovascular collapse, bronchopneumonia, and death.

It is noteworthy that the operative findings disclosed only 2 cases of gangrenous bowel, both with a fatal termination. In one of these an area 2 millimeters wide in the transverse colon was involved in a Richter type of strangulation; in the other, 5 centimeters of small bowel, which was resected. Omentum commonly occupied the sac, and was frequently accompanied by transverse colon. When small intestine was present it was usually jejunum, a point worth mentioning because of the increased danger in high obstruction. In 5 of the 39 cases some other form of hernia was present—inguinal in 4 cases and femoral in 1. This corresponds to the incidence found by Simmons in his series.

The case of the oldest patient, a woman of 88, deserves special mention. A surgeon-in-chief advised incision under local anesthesia, without repair, but later on the same day operation was performed by one of the most capable and enthusiastic of the resident surgeons, who failed to resist the temptation to effect a repair. As a result, the patient collapsed on the operating table and a hurried, sketchy operation had to be improvised. She

recovered, however, and was discharged 45 days after operation. No note was made in the case report as to whether or not the rupture was cured.

The hernias ranged in size from that of a plum to that of a football; 11 were classified as small, the rest as large, usually with a ring from 4 to 6 centimeters in diameter. Two-thirds of the hernias were the size of grapefruit.

The period of hospitalization averaged 23 days in the recovered cases, and 4½ days in the fatal ones.

The predominating symptoms were nausea and vomiting, crampy pain and constipation progressing to obstipation, confirming Thorek's statement that the symptoms of strangulated umbilical hernia are often only those of long standing, uncomplicated hernia in an exaggerated form. Fecal vomiting was rare. The outstanding sign was tenderness of the mass itself. The hernias were tense, hard, and bluish purple or red. Distention was common. Peristalsis if present was easily seen through the thin hernial wall, but this was variable. Gurgling was frequently noted. Ulceration and intertrigo beneath the redundant mass were common. In no case had the ulceration penetrated through the skin and peritoneum, as is sometimes described. Two patients had superficial burns, the result of too vigorous applications of heat previous to admission.

The white cell counts on admission varied from 7000 to 18,000, with an average of 11,000. They were of little aid in diagnosis or treatment.

It may be advisable to consider at this point some of the factors that assist one in determining the proper site of incision in umbilical herniotomy (3, 6, 12, 14). Almost invariably the hernia penetrates the abdominal wall near, but not through, the umbilicus. The presence of the urachus and hypogastric arteries so strengthens the lower edge of the umbilical ring that hernial protrusions make their exit above, in the region of the obliterated omphalomesenteric vein. This potentially weak spot yields under outward and downward strain, and the lateral edges of the recti are pushed outward, with a resulting diastasis. The hard edge of the ring is below, the weak edge above, often with a deposition of fat. The umbilical scar is usually found either at some distance to one side or inferior to the bulk of the protruding mass. Consequently, the hernia, whether for the purpose of repair or that of incision, should be approached from above downward. In a simple incision, this makes the operation technically easier, and obviates cutting through potentially infected, poorly healing skin.

The 2 private cases mentioned, although admittedly not constituting a series, are reported for comparison, and will be described together briefly.

Both patients were women, one 74 years old and the other 73. The former was known to have diabetes. Both were obese, arteriosclerotic, hypertensive, dyspneic, and in obvious pain. In each case the hernia had been present for many years without causing extreme discomfort. The masses were of grapefruit size and irreducible. On admission both patients had had pain, low abdominal cramps, nausea and vomiting, and obstipation of 5 days' duration. Repeated attempts to give enemas were unsuccessful, the fluid failing to enter by gravity; this was correctly interpreted as indicating blockage of the large bowel. There was marked distention, resulting in limited thoracic motility, crepitant râles in the lung bases and slight cyanosis. The hernial tumors in both cases were tender, and peristalsis was not visible. The skin below the masses was moderately inflamed and macerated.

In each case an emergency operation was performed as follows: One-sixth grain of morphine was given by hypodermic injection, and a 1 per cent solution of novocain was infiltrated into the skin and subcutaneous tissue above and to the right of the hernial mass. A linear incision 10 centimeters in length was made in the radius of 11 o'clock. The skin, subcutaneous fat, fascia, ring, and peritoneum were incised. The contents of the sac were inspected and found to consist of viable omentum and transverse colon, and were then dropped back. The peritoneum was closed and likewise the skin, but not the ring or fascia. A large wad of sterile gauze was placed over the opening and held firmly in place by a wide swath of adhesive plaster. The patients were returned to the ward in good condition, and left their beds 2 hours later. Deep breathing and body activity were encouraged at least once every hour during the time the patients were awake.

Convalescence was uneventful in both cases. Within 8 hours after operation there were multiple, watery bowel movements. Gas was evacuated spontaneously and freely. The patients were out of bed daily, and received no sedatives whatsoever except the initial preoperative injection of morphine. The wounds healed by first intention and the patients

were discharged home on the 12th and 10th hospital days, respectively. Both remained comfortable and were not in the least disturbed by the increase in the size of their hernias, to which they had long since been accustomed. They agreed that the result of the herniotomy was wholly satisfactory. A secondary repair was not considered necessary or advisable in either case.

On the basis of the investigation and experience here described, conservative operative management is recommended as the procedure of choice in cases of large umbilical hernia in older patients. In the later decades of life such persons neither want nor require repair of their defects, but seek surgery for the relief of obstruction and strangulation. If the high mortality in this disease is to be reduced, a minimum of surgery is essential. In all bad risk patients herniotomy is the operation of choice, with a two-stage operation in some cases if it seems desirable to repair the hernia, to eliminate failures and reduce morbidity and mortality.

SUMMARY

A resumption of herniotomy as the operation of choice for large strangulated umbilical hernia in old, obese, bad risk patients is advocated as a means of reducing mortality in this disease.

A series of 39 consecutive cases of umbilical hernia in old patients operated on at the Boston City Hospital is analyzed and discussed. The gross mortality was 33 per cent. The mortality in emergency cases was 48 per cent, and increased with advancing age.

Reports of 2 cases in which simple herniotomy without repair achieved successful results are summarized for comparison.

The technique and rationale of umbilical herniotomy are described.

Conservative operative management is the only means of reducing the high mortality in this disease.

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A HALF-RING SPLINT FOR FRACTURES OF THE FEMUR AND TIBIA AND FOR OTHER DISABILITIES OF THE LOWER EXTREMITY

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THERE is need for a splint or a brace which will reduce the weight on the lower extremity in the treatment of a variety of conditions. Fractures of the femur and tibia which have not completely healed, residual paralysis following anterior poliomyelitis, spastic paralysis, osteochondritis of the superior femoral epiphysis, and lesions of the knee joint compromise the majority of these conditions. It is obvious in the use of such a brace for standing or walking that weight removed from the lower extremity must be transferred by the brace from the tuberosity of the ischium through the brace to the ground. For this purpose it has been the general custom for more than a half century to use the Thomas knee or hip splint with a caliper in the shoe, or with an extension beyond the foot. When the brace extends beyond the foot, a raise of several inches is applied to the sole of the opposite foot to remove all the weight from the lower extremity.

The writer made a study of the Thomas ring, which is the primary weight bearing part of the Thomas splint, a number of years ago. In its original form this ring was round, but later Thomas changed the shape to oval. The study showed that for weight bearing in a nonparalytic lower extremity, a round or oval ring could not be made to rest securely under the ischium. Instead, a round or oval ring has the body weight applied to it through the adductor muscles near their origins (chiefly the gracilis and adductor longus) and the medial edge of the inferior surface of the tuberosity of the ischium. When the patient attempts to walk, the ring becomes dislodged from the edge of the ischium by the action of the hamstring muscles at their origin and is displaced into the ischiorectal fossa. Then the weight on the ring is applied through the adductor muscles and the structures in the ischiorectal fossa. If the ring is very large there may be pressure on it by the perineum also.

It is hard to explain the curious custom of Thomas to place the ring of the Thomas splint in the excessive oblique position of 55 degrees from the horizontal. Others have increased this obliquity so that it is not uncommon to see the plane of the ring more oblique than Poupart's inguinal ligament. A disadvantage in this obliquity of the ring is the fact that abduction of the hip is obstructed by the lateral side of the ring contacting the soft parts overlying the lateral surface of the ilium. A possible explanation seems to be that since it is technically impossible to fit a round or oval ring securely under the ischial tuberosity, bracemakers have empirically placed the ring in an oblique position to have a concave segment of the ring to act as a sling under the adductor muscles and ischiorectal fossa, in an effort to relieve some of the discomfort. Only a small part of the weight which is normally carried by a lower extremity can be borne by the adductor muscles, the ischiorectal fossa, or the perineum on account of the pain caused by pressure on the padded metal ring of the Thomas splint. The discomfort can be relieved by shortening the brace until practically no weight is carried on it, this being a common device of some bracemakers who are harassed by surgeons in their vain effort to make an oval ring fit securely under the ischium. The patient bears a large part of his weight on crutches to relieve the pressure of his weight on the ring. For these reasons a Thomas ring splint has not been used by surgeons in many cases when a splint to remove weight from the lower extremity is indicated.

Another obvious difficulty with the Thomas ring splint has been its use with a caliper in the shoe. The caliper is made by bending the lower ends of the side rods at a right angle and fitting them into a tunnel in the heel of the shoe. This is a rather crude means of making a joint in the splint which is supposed to move in the same axis as that of the ankle joint. However, the caliper joint moves eccentrically so that its axis is approximately 6 centimeters distal to the axis of rotation of the ankle joint when applied to an adult of average size. When the caliper splint is used for walking, its eccentric caliper joint in relation to the axis of the ankle joint will cause the entire brace to move up and down on the lower extremity. The side bars are relatively shortened on the lower extremity as the ankle is plantar flexed or

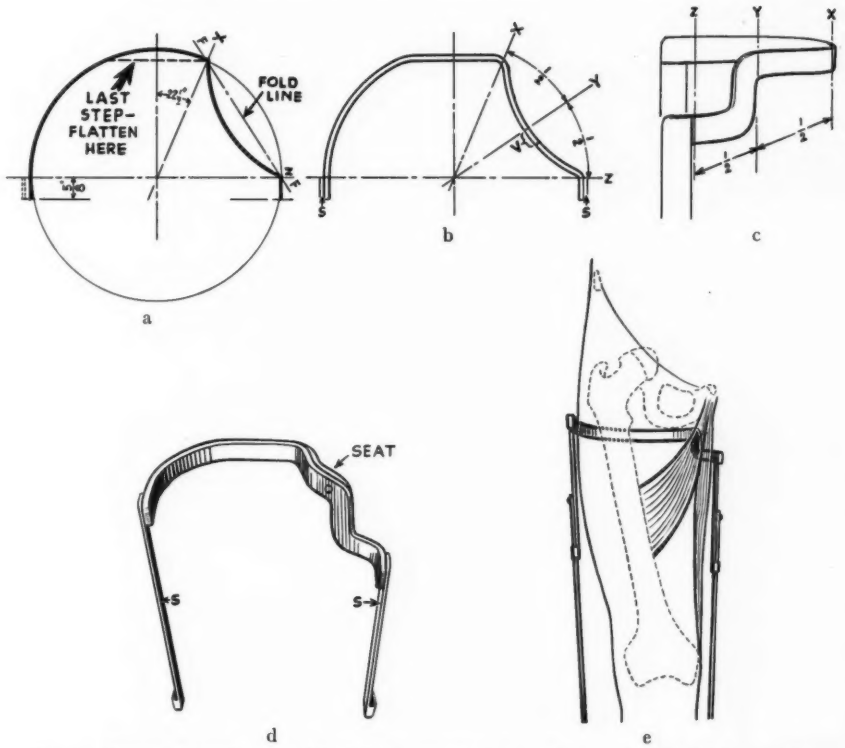

Fig. 1. a, Bracemakers diagram with circle representing circumference of right thigh at perineum. Heavy line indicates pattern for metal half-ring with ends extended for width of side bars. A 22½ degree arc is marked from the posteromedial quadrant. The arc *XZ* is reversed in its curve by folding the paper along fold line *FF* after circle is cut from paper drawing. b, Soft iron 3/16 inches by ⅝ inches bent to shape of pattern. Arc *XV* represents seat for ischium. *V* indicates position of vertical bend downward for 1½ inches, the remaining part of the arc *VZ* being horizontal. c, Medial view showing arc *XV* as the seat for the ischium and the arc *VZ* which is the vertical and anterior horizontal section of the ring. d, The metal half ring with side bars *S* attached. The seat section for the tuber ischii has an extra thickness of metal in the concavity of the curve which is held in place by two rivets. e, The half ring in position under the tuber ischii. The adductor muscles escape pressure by passing through the space anterior to the seat and the vertical section.

dorsiflexed. The side bars also move anteriorly and posteriorly in relation to the leg during these movements of the ankle joint. Therefore, a walking splint, with a caliper in the shoe and an oval ring for weight bearing by the ischium, does not conform to the principles of mechanics and should not be used as a surgical appliance.

In an effort to overcome the difficulties encountered by the use of the Thomas ring and caliper, I have endeavored to work out an ischio-bearing brace which fits positively under the tuber ischii with side bars extending to the ground, and with joints in the side bars which work in the axis of rotation of the ankle joint.

The member or part of this brace which provides a bearing surface for the ischium necessarily must fit around the upper part of the thigh, as a place to anchor the brace as a whole. However, the facts in the foregoing explain why an oval ring is far too simple in design to provide a seat for the ischium which is located deep in the soft parts of the buttock and is not superficial.

In the previous study the writer worked out a weight bearing surface on a brace which fits under the ischium in most cases, but the problem of pressure on the adductor muscles at their origin was not solved. Many of the cases used in that study were those of patients who had a residual

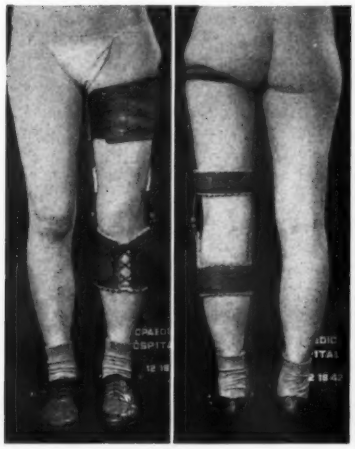

Fig. 2.

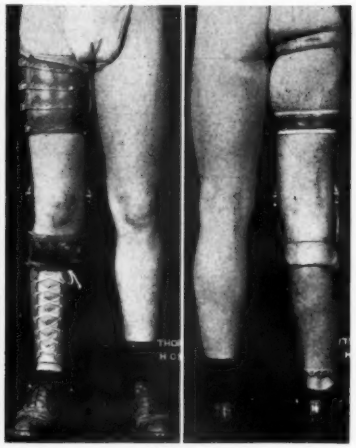

Fig. 3.

Fig. 2. The brace applied to a patient 8 weeks after a transverse fracture of the middle of the shaft of the femur, treated primarily by skeletal traction.

Fig. 3. The brace applied to a patient 6 weeks after a transverse fracture of the shaft of the tibia. A molded leather cuff extends from the tubercle of the tibia to the malleoli. This cuff is not necessary in all fractures of the tibia.

poliomyelitis and in whom the postural tonus of the thigh and gluteal muscles was poor or these muscles were partly paralyzed. In these cases pressure on the adductors was not a serious problem. The use of the cadaver in the early study was helpful but the rigid muscles were deceptive when compared to those of a subject with well developed active muscles.

Therefore, changes in the shape of the original bearing surface for the ischium have been made as a result of more study and experience. The new part of the brace which provides a seat for the ischium has no resemblance to any known shape or object, as in the case of the innominate bone. It is called an ischio-bearing half-ring for want of a descriptive name. This rigid part is a padded flat strip of metal which fits over the posterior half of the junction between the thigh and the buttock. Part of it is bent laterally from the posteromedial side to fit under the tuber ischii. Another bend is made on the medial side of the metal in an inferior direction to allow an open space to prevent weight bearing by the adductor muscles. This ischio-bearing metal band is covered with felt ¼ inch thick and leather, and is held in place by the side bars of the splint and by a wide leather band at least 6 inches wide, which is buckled between the side bars on the anterior aspect of the upper thigh. The broad leather spreads the pressure which is required to pull the seat of the half-ring under the ischium. The thickness of the felt and leather is ignored in the measurement because the subcutaneous fat is displaced sufficient to allow for it. A leather band about 2½ inches wide is placed between the side bars on the posterior aspect at the middle of the thigh. The function of this band is to prevent the pressure of the anterior thigh cuff from forcing the knee into hyperextension. Formerly we used metal inside of this posterior cuff. However, the metal interfered with the chair in sitting and was a source of discomfort and annoyance to the patient.

Joints are placed in the side bars in the axis of the knee joint, as in other types of splints and braces. However, the location of the joints at the knee are not so important because when used for weight bearing these joints are locked with slip-locks which can be loosened to flex the knee when the patient is in the sitting position. If the knee joints are placed lower than the axis of the knee joint the side bars will not project under the trouser leg in an unsightly manner.

The calf band of the brace is extended in a proximal direction in the part anterior to the side bars so that it makes pressure on the tubercle of the tibia to prevent flexion of the knee when the patient is standing.

The ankle joints in the side bars should be placed so that they work in the axis of rotation of the ankle joint. This axis is just above the joint between the talus and the calcaneus, this being

about 5 centimeters above the inferior surface of the patient's heel.

In the construction of this splint, the following procedures are necessary. The circumference of the patient's thigh at the perineum is measured with a steel tape. The radius of a circle with the same circumference is calculated. To make a pattern, a circle with this radius is drawn on a sheet of paper on a drawing board. (Fig. 1, a). With a T square 2 diameters are drawn at right angles across the circle to make four segments. Two adjacent quadrants are designated to simulate the posterior half of the junction between the thigh and the buttock. One of these segments represents the posteromedial, the other the posterolateral side of this region. An arc of 22½ degrees is marked with a protractor in the posteromedial quadrant from the line separating it from the posterolateral quadrant. Then the paper is removed from the drawing board and the circle is cut out with a pair of scissors. The edge of the circular disc of paper is then folded over from the posteromedial quadrant in its medial 67½ degrees (line *FF*, Fig. 1, a), the circumference of the circle being reversed in this part. A line is drawn on the paper to mark the reversed curve, and the paper is cut to follow this line. The remaining part of the paper with the two posterior quadrants of the disc is pasted to a piece of cardboard which is cut to the shape of the paper. This is the pattern to be used by the bracemaker.

The bracemaker takes a length of band iron 3/16 or ¼ inch thick and ⅝ inch wide and bends it with a vise, hammer, and forge to conform to the shape of the pattern as indicated by the heavy line in Figure 1, a. A vertical bend is made as shown in Figure 1, b, c, and d. The vertical bend indicated at bracket *V* in drawing b is in the arc *XZ*. This vertical portion of the metal is 1½ inches long for adults and relatively shorter for children. The metal is bent horizontally then to conform to the remaining curve in the arc *YZ*. Sufficient metal must be allowed at each end of the half ring for riveting and welding to the side bars, *S*. The ring is flattened posterior as a last step so that it will not roll on the chair when the patient is sitting. In the arc *XY* which is the seat for the ischium, the metal should be made thicker for the seat by applying another section of the 3/16 or ¼ inch by ⅝ inch metal to the concavity of the curve by the use of two rivets to hold it in place. This should be set a little high and then the entire seat section should be buffed down on its superior surface so that it is horizontal when the ring is attached to the side bars with 10 degrees' elevation from the horizontal on the lateral side.

Fig. 4. A roentgenogram of the half-ring used on a brace for ambulatory treatment in a case of Legg's disease. The space between the seat and the tuber ischii is obviously occupied by soft parts and padding.

The side bars *S* (Fig. 1, b and d) are made of ⅛ inch by ⅝ inch spring steel. They are placed anterior to the half-ring which is set obliquely so the lateral side is 10 degrees higher than the medial side. The side bars should be adjustable for length by overlapping two sections above the knee, and below the knee also if the patient is a child.

When the brace is being applied to a patient it is important to pull the skin and subcutaneous fat overlying the tuber ischii in an inferior direction to prevent compression and pinching of a fold of these tissues between the half-ring and the bone.

The side bars should be extended and made sufficiently long to elevate the sole of the heel of the patient ¼ to ½ inch above the heel of the shoe so that there is no weight bearing by the heel. If there is any doubt about weight on the heel this can be determined by a lateral x-ray picture through the shoe with the patient standing with the brace applied. The shoe should be laced last after the brace is applied, and then it will be seen

that the lacing is wider apart than the lacing in the opposite shoe, indicating an elevation of the heel and dorsum of the foot. The amount of weight removed from the lower extremity is determined by the condition for which it is used.

APPLICATIONS

1. Fractures of the femur and tibia when union is incomplete, when there is a delayed union, and in nonunion after bone transplantation. When a reasonable amount of callus is visible in a roentgenogram the brace may be applied to allow a small amount of weight to be applied through the forefoot but to prevent bending of the bones at the fracture side by excessive weight. The splint is useful in fractures of the shaft of the tibia instead of a cast and walking iron which should never be used in such cases. The splint can be used in all types of fractures of the femur including fractures of the femoral neck when there is a delayed union. When fractures are almost completely healed the slip-locks at the knee can be kept released to allow movement in the joint when walking; the brace will continue to give some protection.

2. Residual anterior poliomyelitis, in which there is severe paralysis of the thigh and gluteal muscles. It is especially useful in patients with an almost total paralysis of the lower extremities as in dangle legs. In these cases it is not necessary to elevate the heel above the heel of the shoe. The brace should be sufficiently long to prevent undue flexion or hyperextension of the knee. The trunk is stabilized by resting the ischium on the half-ring seat.

3. Spastic paralysis with severe involvement of one or both lower extremities. The brace is used to prevent undue flexion contracture at the knees and hips. The patients can get about with or without crutches. By maintaining the knee in an extended position the brace also helps to prevent flexion contracture at the hips because it helps the patient to stand and walk.

4. Osteochondritis of the superior femoral epiphysis or of the acetabulum. This brace has been used in cases of Legg-Perthes disease, in cases of slipping femoral epiphysis, and in osteochondritis of the acetabulum after the acute stage was treated by recumbency with traction or in plaster spicas. It allows these patients to be ambulatory with an assurance that they are not being made worse by weight bearing. In our experience healing occurs with less deformity because the brace allows function with a minimum of weight on the joint structures.

5. Knee joint lesions. Following arthrodesis of the knee in tuberculous disease of the joint the brace is used to allow partial weight bearing and prevent flexion or other deformities after removal of the plaster spica during the process of fusion of the femur and tibia. This brace has been used in some cases of atrophic arthritis of the knee joint to prevent flexion contracture and restore the function of walking.

SUMMARY

1. A splint or brace extending from the tuber ischii to the ground is useful to remove all or part of the body weight from the lower extremity in a number of pathological conditions, fractures of the femur and tibia being the most common of any of these.

2. An encircling band around the thigh at its proximal end must provide a seat for the tuber ischii. However, a simple round or oval ring cannot fit under the tuberosity of the ischium because the arc nearest to it is concave instead of being convex.

3. A padded half circle of flat metal, bent to fit anatomically under the tuber ischii, is described for application to side rods which extend to the ground through the shoe heel. The half-ring is held in place by leather which is buckled between the side bars anteriorly.

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RECONSTRUCTION OF BREAST DEFORMITIES

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BREASTS are deformed, according to the female patient, either because they are hypertrophic—or in rarer instances—too small. The etiology of either type is not well understood. It is probably the result of endocrine dysfunction. In the hypertrophic type, additional factors such as pregnancy or obesity may lead to the deformity.

McIndoe divides the hypertrophic forms in 5 types: (1) Long, heavy, pendulous breasts with hypertrophy of the most dependent glandular portion, characteristic of the adolescent girl of otherwise normal build. This is probably purely endocrine in type. (2) Broad, heavy breasts associated with obesity and aggravated by pregnancy. This is probably of more complex endocrine origin. (3) Sac-like dependent breasts following obesity reduction of the second variety or multiple pregnancies in the first. (4) True gynecomastia. Marked hypertrophy of the glandular elements of the breasts results in one of enormous proportions. These cases are not common, but are purely glandular in origin and related to type one. (5) Asymmetry.

A number of operations have been devised for reconstruction of breast deformities. An exhaustive and well illustrated review of the various operations has been published by Biesenberger and most recently, by Thorek. Each method has advantages and disadvantages.

OPERATION FOR HYPERTROPHIC, PENDULOUS BREASTS

The reconstructive operation for pendulous breasts should fulfill two purposes: first, correct the deformity; second, maintain the function of the gland.

a. One stage operation for moderately hypertrophic breasts (Lexer's method) (Fig. 2). This method has been described previously by the author (7). The method is applicable for moderately hypertrophic breasts or those breasts which consist of a flabby sac of skin with scanty breast tissue at the bottom. It is performed on both sides at one sitting.

In large hypertrophic pendulous breasts, however, a two stage procedure is safer so as not to endanger the circulation of the areola. In those cases Lexer advises resection of some of the breast tissue during the first stage of his operation and of the other part in a second stage four weeks later. This means two major operations. To change the second stage from a major to a minor stage, I devised a procedure a description of which follows.

b. Two stage operation for hypertrophic, pendulous breasts (author's method) (Fig. 1). The blood supply of the breast is derived from three sources: branches of the arteria axillaris, of the mammaria interna, and arteriae intercostales. According to Cruveilliers, Kaufman, and others, the third and fourth branches of the arteria mammaria interna carry the main blood supply, not only to the gland but also to the areola. While the branches of the arteria axillaris supply only the lateral superficial parts of the breast, the intercostal arteries are insignificant (Anson, Wright, and Wolfer). Thus, the areola receives its blood supply from beneath —from branches of the arteria mammaria interna —and also from the surrounding skin. If the areola is separated from the surrounding skin but left attached to its base, a sufficient blood supply is guaranteed from beneath. If, however, in addition to the skin incisions, much breast tissue needs to be removed, the deep blood supply of the areola may become insufficient unless proper precautions are taken, i.e., resecting only the lateral parts of the breast tissue, leaving the median half intact to form a median pedicle (Biesenberger, and Gillies and McIndoe); leaving the areola attached to an epidermis freed pedicled flap (Schwarzmann), etc.

A two stage procedure (Fig. 1), however, seems to me the safest way to counteract any variability of the blood supply and thus to avoid nipple necrosis. The simplest way to counteract any circulatory disturbance of the areola is the formation of a bridge—or double pedicled flap—in which the distal pedicle is the areola, which remains anchored to its base. The flap comes to lie above the areola and consists of that part of the skin which in Lexer's procedure, is removed (compare with Fig. 2a–d). Such a flap carries sufficient circulation to safeguard the viability of the areola if much breast tissue must be removed. The flap is removed in the second stage of the operation about two weeks later.

The operation is carried out as follows (Fig. 1, a–e): the first stage is performed under general anesthesia; the patient is in a half sitting position. The two points to which the nipples are to be transferred are marked with a drop of methylene

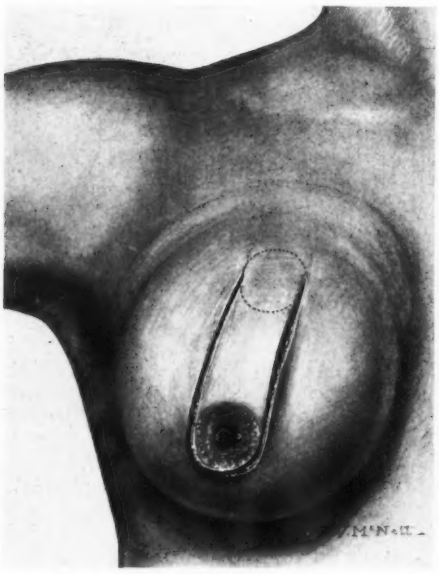


Fig. 1a.

Fig. 1b.

Fig. 1. a, The point to which the areola is to be transferred is marked with a drop of methylene blue. An ordinary medicine glass is used as a pattern and placed over this point and its rim is outlined with the dye. The medicine glass is now placed over the nipple and its rim outlined on the areola. The most lateral and median points of both outlines are connected with each other by an incision. b, Between both incisions the skin and subcutaneous tissue (not the areola) are undermined to form a bridge flap. Another incision is carried around the lower half of the areola. Note outline of curved incision in lower half of breast.

blue injected intracutaneously. An ordinary medicine glass placed over this point is used as a pattern and its rim is outlined with a dye. The medicine glass is now placed over the nipple and its rim is outlined on the areola; the most lateral points of both outlines are connected with each other by an incision. Another incision parallel to the former connects both median points. Between both incisions, the skin and subcutaneous tissue (not the areola) are undermined to form a bridge flap. An incision is now carried around the lower half of the areola; after the surrounding skin is undermined and separated, the areola, which is left in contact with its base, is lifted upward and connected with the upper pedicle of the bridge flap with sutures. Then it is fastened to the surrounding skin with subcutaneous and skin sutures. Both halves of the bridge flap are fastened to each other with a few skin sutures. The next step consists of an incision of the skin beneath the areola in continuation of the upper cuts, not parallel, but in diverging curves; the terminal points of the incisions should lie at least one inch above the mammary fold, not within the fold, because the fold of the breast after reduction of its size becomes displaced upward. Between both incisions lies a triangular-shaped piece of skin which is dissected downward and forms a flap (center flap) for later use. The next step consists of separation and blunt dissection of the skin from the lateral and median lower halves of the breast, care being taken not to carry the dissection too far. The hypertrophic parts of the breast are now bulging more laterally and median than below the areola. The parts bulging lateral to the areola are now grasped and excised in a wedge-shaped form, as outlined in Figure 1d. The same is done on the median side. Thus, a center bloc of breast tissue is left, to which the lateral and median wound edges are attached with heavy, chromic catgut sutures; in other words, the center part which carries important vessels is left intact; it is simply lifted upward. If it is still bulging, it may be shaved off to proper size. The lowest lateral and median sutures attach the breast to the pectoral fascia. The surrounding skin is now trimmed to conform to the lower half of the areola and breast and sutured together with two rows of sutures

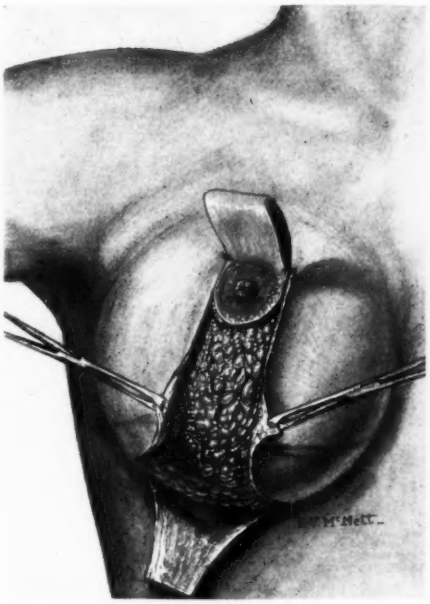


Fig. 1c.

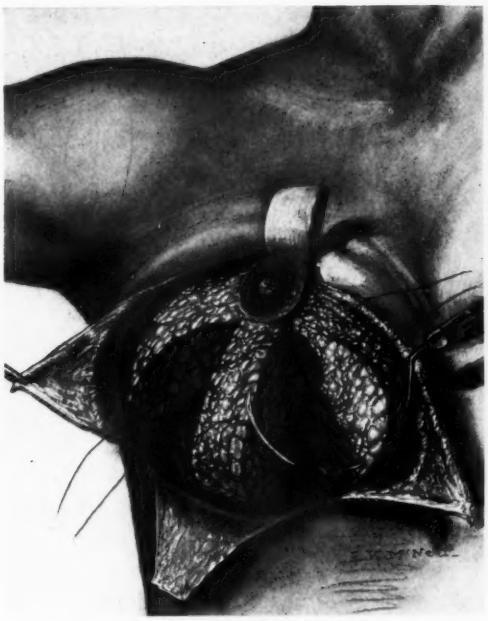


Fig. 1d.

Fig. 1. c, After the undermining and separation of the surrounding skin the areola which is left in contact with its base is lifted upward and connected with the upper pedicle of the bridge flap with sutures. The next step consists of an incision of the skin below the areola in continuation of the upper cuts, but in diverging curves. The terminal points of the incisions should lie at least 1 inch above the mammary fold because the fold of the breast after reduction of its size becomes displaced upward. A triangular shaped piece of skin between both incisions is dissected downward to form a flap for later use. d, Separation and blunt dissection of the skin from the lateral and median lower halves of the breast. The hypertrophic parts of the breast bulging laterally and median are grasped and excised in a wedge shaped form. Thus, a center block of tissue is left to which the lateral and median wound edges are attached. This center part acts as a buttress and a carrier for important vessels. If it is still bulging it may be shaved off to the proper size. The lower sutures attach the breast and the pectoral fascia. e, The surrounding skin is now trimmed to conform to the lower half of the areola and breast and is sutured together with 2 rows of sutures (subcutaneous and skin sutures). The bridge flap is separated in the same stage and the areola adjusted in place if clamping of the flap does not result in discoloration. If, however, discoloration becomes evident, this flap is removed 2 weeks later.

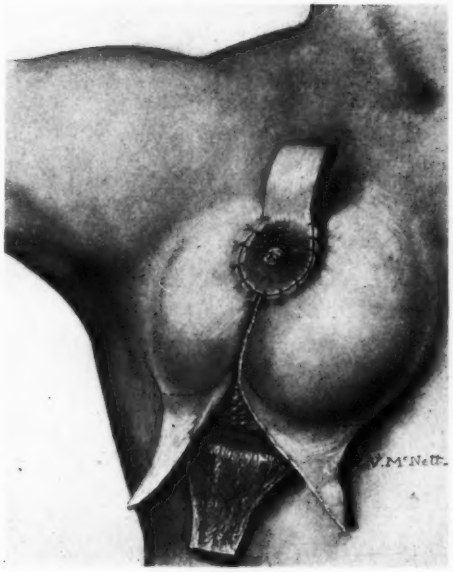


Fig. 1e.

(subcutaneous and skin sutures). Finally the center skin flap is trimmed and sutured to the lateral and median flaps. A drain is placed in the lateral corner. The same operation is performed on the other side. A firm compression dressing is applied to both breasts, care being taken that the pedicles above the areola are free from any pressure; otherwise, necrosis of the nipples may result.

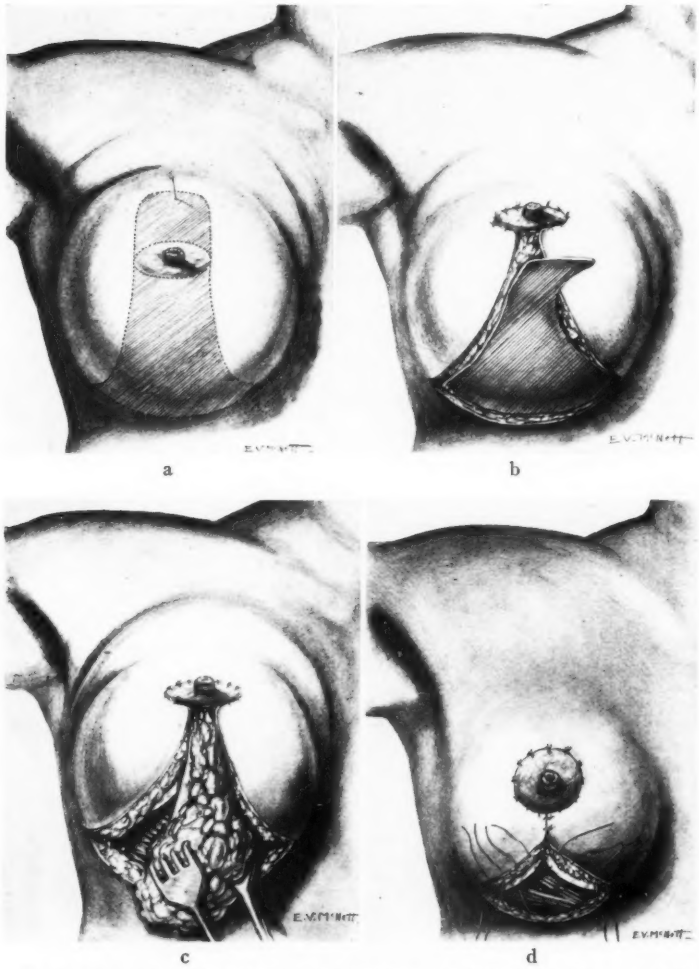


Fig. 2. One stage plastic of the breast: a, incision around the nipple; the parts of the skin to be removed are outlined; the pin marks the place where the nipple will be transferred. b, The nipple is transferred into the upper corner of the wound. c, Excision of the bulging tissue. d, Closure of the wound in layers. (Courtesy, *Archives of Surgery*, 1939, 38: 113.)

The second stage is performed after about 2 weeks. The bridge flaps are clamped and if there is no discoloration of the areola, the flaps are removed under local anesthesia, first from the areola, then from the upper attachment. The areola is then sutured to the upper wound edge.

The same operation can be modified in various ways:

a. In not too extreme cases, one may clamp the bridge flap at the end of the operation, and if there is no discoloration of the areola, the flaps may be removed in the same sitting.

b. In very extreme cases, however, it may be better to raise the bridge flap and to circumscribe the lower half of the areola with an incision first, and to suture flap and areola back again, i.e., delay the flap to assure better circulation. The main operation is carried out after 3 weeks and separation of the flaps is performed 2 weeks subsequently.

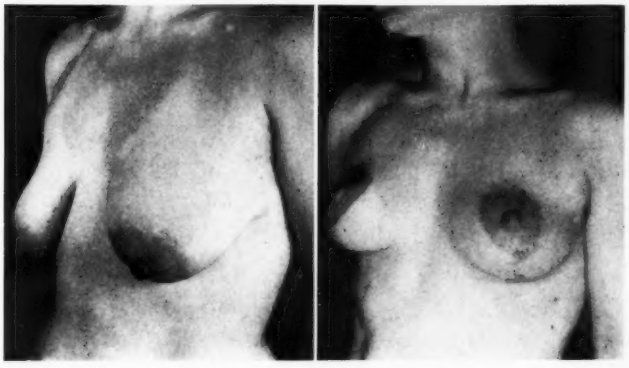


Fig. 3. a, left, Patient, aged 29 years, married, with 2 children, has pendulous breasts. b, One year after a one stage breast plastic.

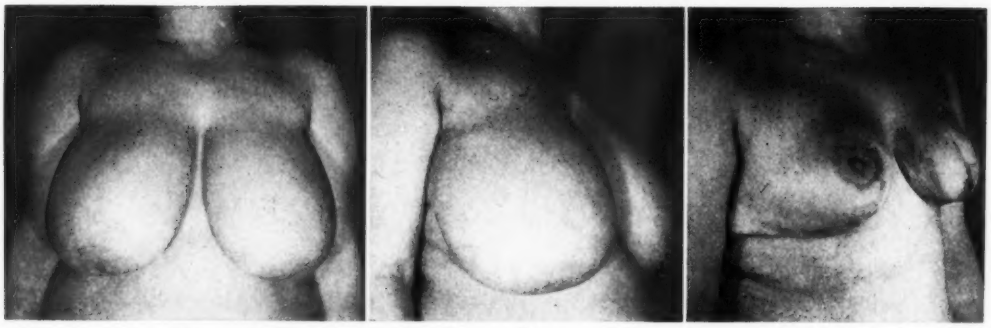
c. There is another possibility. If, due to reasons as stated later, a plastic amputation of the breast is performed, one may be able to transplant the areolae. If this is planned, the bridge flap is raised and returned to its base in the first operation as here described. In the main operation 3 weeks later, the flap is raised and the distal pedicle, i.e. the areola, is separated from its base, thus converting the bridge flap into a single pedicle flap with the areola at its peripheral end. The plastic amputation is now carried out and at the end of the operation, the areola is sutured into the upper wound edge; the picture now resembles that which is seen in Figure 1, e; separation of the bridge flap is carried out 2 weeks after amputation.

d. There is still another possibility of using the bridge flap; this was discovered through a rather sad experience. The following case presents an instructive example. This patient had very large, hypertrophic, pendulous breasts (Figure 5). A three stage operation was performed as described. The usual pressure dressing was applied, care being taken to leave the flaps free of any pressure. Some bleeding occurred after the operation, and the attending nurse called the house physician, asking him for advice. She was told to reinforce the dressing. When the patient was seen the next day, one turn of the figure-of-eight dressing included the lower half of the left bridge flap, resulting in complete necrosis of the left areola. Later on, the areola was excised and the upper half of the bridge flap which remained intact was used to cover the defect. Thus, it may be noted that, if in spite of all precautions which are taken, the areola or a portion of it becomes necrotic, parts of the flap may be used to cover the resulting defect.

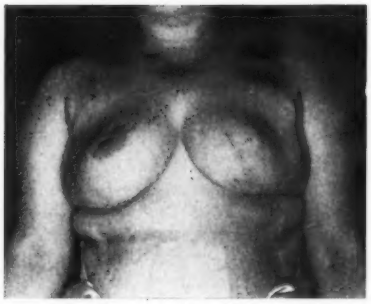
PLASTIC AMPUTATION

Under plastic amputation is understood an operation by which the greater parts of the breast, including the areola, are removed and the remaining parts of breast tissue and skin are used for recreating a natural shape. Indications for such an operation are various: enormously large breasts (hypertrophia vera, first described by Billroth); large, hypertrophic breasts with poor circulation; large breasts without function. It has been feared that a plastic amputation may lead to cystic degeneration and other disturbances; this can hardly be true in those breasts which are without function. Patient, 30 years of age, had very large breasts, both were cyanotic and displayed several flat scars from superficial ulcerations (Fig. 6). She had one child, but did not lactate at that time. A bilateral plastic amputation was performed. Five years later she delivered another child; neither breast showed the slightest evidence of function. There are cases reported in literature (Hollander, Sebening, Schwarzmann) in which

Fig. 4. a, left, Patient, aged 19 years, hypertrophic pendulous breasts had a two stage breast plastic performed. b, The result 2½ years after the operation. Patient wore brassiere size 44 before operation, now wears size 34.



a b c



d

Fig. 5. a, Marked breast hypertrophy reduced in a three stage operation: first, mobilization of double pedicled flap and suturing it back again; 3 weeks later, performance of main operation; 12 days later separation of right pedicle. The left areola became necrotic. Some bleeding occurred after the operation; the attending nurse reinforced the figure-of-eight dressing upon advice of the house physician. When the patient was seen the next day one turn of the dressing had constricted the lower half of the bridge flap. The upper half was used to close the resulting defect. c, Patient 6 weeks after operation; d, 1 year after operation. General loss of weight by dieting.

even in functioning breasts from which the nipples were absent no pathological disturbances occurred during and after pregnancy. Some of the cases were followed up for many years. In one of the author's cases the function of the gland could be promptly stopped after administration of 5 milligrams of stilbestrol three times a day soon after delivery.

The operation is performed similar to the one stage operation after Lexer (Fig. 2). The point to which the nipples are to be transferred is marked. From this point, two curved diverging incisions are made similar to those in the ordinary one stage operation (Fig. 2b–d). Skin, nipples, and breast tissue lying between these incisions are removed *en bloc*. The resulting wound is closed in layers.

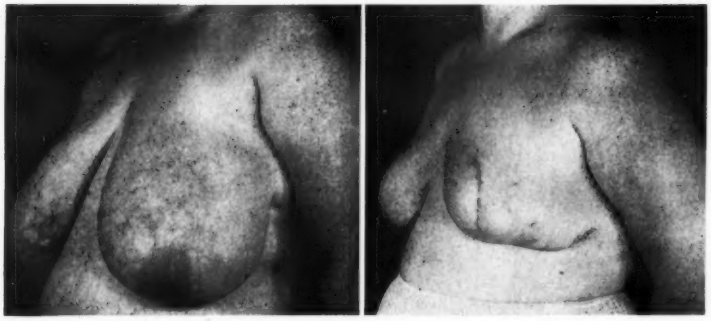


Fig. 6. a, left, Woman, aged 30 years, with marked hypertrophy of breasts: note enlarged veins, scars, and trophic ulcer; patient had 1 child, did not lactate at that time. The local disturbance of circulation was a contraindication for a breast plastic. A plastic amputation was performed. Five years later she delivered another child; neither breast showed evidence of function.

In some cases, the areola may be preserved and transplanted in a way as described previously, or, according to Thorek, may be excised from its underlying structures and transplanted as a free graft into the upper wound corner after this place has been properly excised and prepared to receive the graft. Thorek emphasizes the importance of making the excised hole smaller than the graft, thus allowing for shrinkage of the graft.

RECONSTRUCTIVE OPERATION IN SMALL BREASTS

Indications for such an operation are: smallness of breasts due to removal of breast tissue (cystic mastopathia, tumor), and genuine small breasts (hypomastia). Czerny, as far as can be ascertained, was the first who performed a reconstructive operation for correction of a small breast. For an actress, from whom cystic tissue of the left breast had been removed, he replaced it by a lipoma which the patient had accidentally in her lumbar region. The breast remained well formed, the lipoma did not grow.

If the breast deformity is unilateral as it may be in postoperative cases, and the other breast is large, the large breast may be reduced by a breast plastic and some of the resected tissue transplanted into the small breast. If this is impossible, a fat tissue graft should be used. In genuine small breasts (hypomastia) hormone treatment should be given a trial (MacBryde). If it fails, fat tissue should be transplanted. The graft is preferably taken from the thigh. It is advisable to take the graft two-thirds larger than required to counteract degeneration and shrinkage. Furthermore, it is advisable to remove some of the underlying fascia with the fat tissue graft. A recent experience makes me believe that the fascia may limit the shrinkage of the graft (Fig. 7).

Four years ago a married woman, age 26, came to me with the request to increase the size of her breasts. I told her that such an operation is possible but not advisable without first having tried conservative methods in the form of hormone treatment and increase of weight. The family doctor was informed and he treated the patient along this line. She returned to me 1 year later and stated that she had gained 15 pounds, but in the gluteal region rather than in the breasts. The breasts were still atrophic; they also were functionless. She had one child, but did not lactate at that time. The operation was performed.

From an incision in the mammary folds the breasts were separated from the pectoral fascia. A large piece of fat tissue was removed from the lateroposterior surface of the left thigh and transplanted between the left breast and pectoral fascia. A similar piece of fat was removed from the right leg, accidentally, together with some fascia lata and transplanted into the right breast. The wounds were closed in layers. All wounds healed primarily. The follow-up examination 9 months after the operation revealed shrinkage of the left graft about two-thirds of its size, while the right graft showed hardly any shrinkage. While the donor area of the left leg was filling up again, the scar on the right leg remained depressed. The explanation for this phenomenon may lie in the fact that fat plus fascia was transplanted on the right side, while no fascia was used on the left side. The left breast was operated on again; more fat tissue together with fascia was transplanted. Only slight shrinkage of the graft has occurred since.

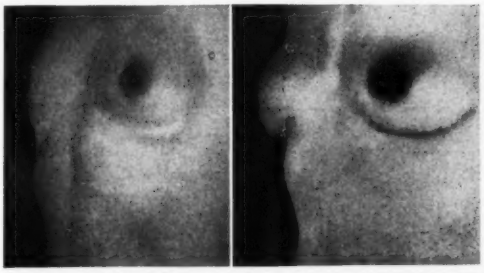


Fig. 7. a, left, Patient with small, functionless breasts (hypomastia); hormone therapy and gain of weight failed to increase size of breasts. b, Fifteen months after transplantation of fat and fascia lata from thighs beneath breasts.

SUMMARY

Reconstructive operations for correction of various forms of hypertrophic and atrophic breasts are described and illustrated.

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USE OF FASCIAL SUTURES IN INGUINAL HERNIA

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THE importance of fascial sutures in the repair of difficult inguinal hernias with large parietal defects can hardly be exaggerated. Moreover, their usefulness has steadily expanded from their initial employment in hernioplasty to almost all allied surgical fields. Fascia is used in the mobilization of stiff joints and the stabilization of subluxated ones, in the retention of fragments in certain types of fractures, particularly of the patella and olecranon process, in the re-establishment of incontinent sphincters, in the suspension of ptosed kidneys, and occasionally in internal neurolysis.

The superiority of fascia over catgut, silk, and other nonviable sutures lies in the fact that it possesses great tensile strength, is nonirritating, remains viable for many years and may be used where there is special need for tendinous, ligamentous, or fascial replacement. Why it has been so slow in attaining its present enviable position may be attributed to lack of knowledge concerning its histological evolution in its new environment, the mechanical difficulties experienced in its proper placement necessitating the development of large-eyed and more sturdy needles, and the obstacles encountered in the procurement of the free fascial suture.

To understand better the paucity in the general acceptance of living sutures it is necessary to recall, for comparative purposes, the extent of contemporary development of the allied sciences, histology, pathology, physiology and anatomy which were not co-ordinated then as they are today. It was not the custom, nor was it possible in that era, to do extensive research on the plausibility of theory. Our thinking was directed more toward practical realism and clinical application. Laboratory research had not developed to the point where it was serving as the proving ground of new ideas and new techniques.

McArthur in 1901 was the first to conceive and make practical application of a living suture. He employed a pedicled suture taken from the cut edge of the external oblique aponeurosis which he used as a running suture in apposing the conjoined tendon to Poupart's ligament as the first step in the repair of an inguinal hernia. Despite the success attending McArthur's innovation and the soundness of the principle which was destined to play an important rôle in plastic surgery, the profession was loath to accept it because as yet the universal question concerning the fate of the autogenous suture could not be answered unequivocally and quite naturally there was some basis for the existent skepticism of many surgeons.

Almost a decade later Kirschner in 1909 performed some experiments using tendinous and fascial grafts and observed that these transplants retained their gross and histoiogical characteristics. This was followed by more careful studies of fascial sutures by Lewis (11, 12) and his associates in 1916 and 1917. However, autogenous fascioplasty received its greatest impetus from the publications of Gallie and LeMesurier (3, 4, 5). The experimental observations of these two investigators with their carefully followed representative group of cases, many of them having been unsuccessfully operated upon by other methods were so convincing and the results so gratifying that the evidence seemed almost irrefutably in favor of lasting viability of the sutures. Statistical reports from many sources have corroborated the principles of Gallie's technique, which is generally accepted as the procedure of choice in the repair of recurrent and difficult hernias. However, it is unfair to disregard other essentials of the operation and assume that the fascial suture, alone, is a panacea for all hernias. Nevertheless, it is a decided improvement over other contemporary methods and offers cures to a group of patients who hitherto had been considered hopelessly incurable, many of them otherwise physically strong.

On the other hand there have been adverse reports on the use of living sutures with higher recurrence rates, and a few surgeons have abandoned their use. Yet, in spite of an occasional unfavorable report, living sutures are gaining in popularity. I am referring to viable fascial strips as distinguished from preserved dead ox fascia of Koontz and Nageotte and subsequently applied to man by Glasser, Egan, and others. Moreover, it has been demonstrated that heteroplastic grafts behave like catgut and have a short survival period.

The fascial technique has also been condemned on the ground that owing to the size of the suture

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Fig. 1. Lower extremity; anatomical relationship of iliotibial tract.

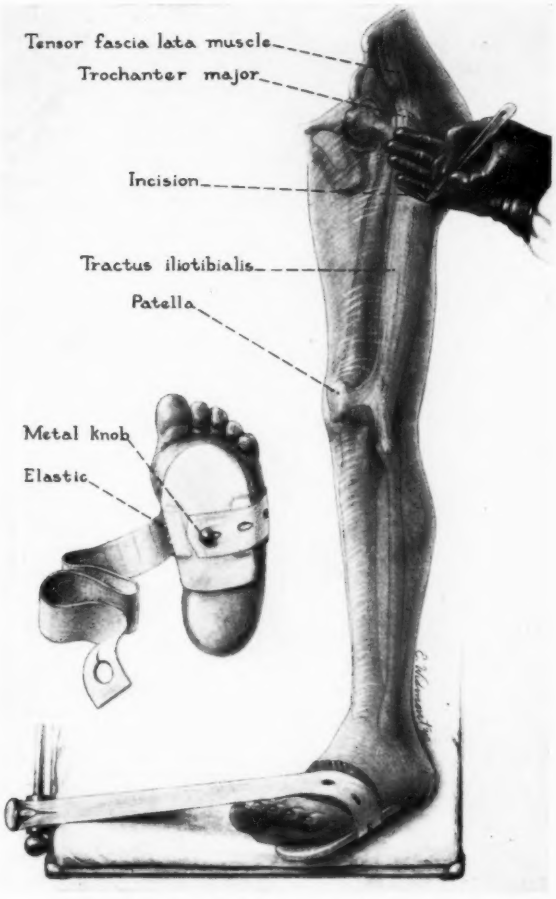

Fig. 2. Detail of the sandal in use; the location of the incision is also illustrated.

it is cumbersome to handle, produces trauma, and sometimes tears the tissues. This accusation is true in a relative sense only. It is assuredly untrue clinically provided the proper sized suture is selected and care is exercised in its placement. The needle should be passed, clearing the inguinal ligament, reversed, and passed back, forming a vertical loop which can be done without the knot hanging as it is drawn through the ligament. If the suture is forcibly passed through the ligament, out and in with a single stroke, it is more likely to produce tearing and not infrequently the suture is pulled with such violence that it is jerked free of the needle. Such practice brings disrepute on a valuable method. Another point worthy of mention is to insert the needle under the loops of the first fascial suture and not through the ligament when imbricating the aponeurotic flaps.

Fascial sutures may be either pedicled or free depending upon the nearness of the donor site. The former is procured from adjacent structures and does not require an additional incision. Those who have sponsored this source of obtaining the suture include McArthur and Joyce, who used a single suture; Robins and Sachs, who prefer a double suture taken from the lateral and median edges of the external oblique aponeurosis; and Hodgkins, who employs multiple interrupted sutures raised from the anterior sheath of rectus. A disadvantage of pedicled sutures is the chance of

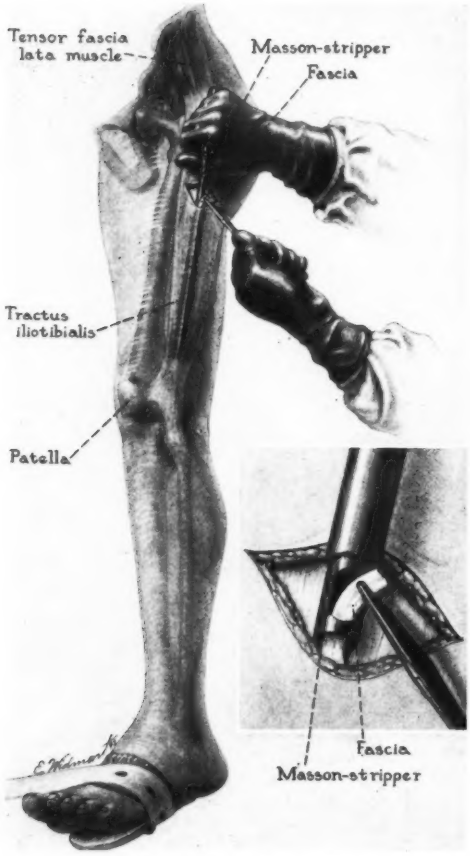

Fig. 3. Extraction of fascial strips with the Masson stripper.

compromising the function of the contributing stratum and indirectly jeopardizing the repair by substituting a potentially vulnerable area in lieu of the original hernial weakness. Another disadvantage, although remote, is the possibility of underestimating the extent of the parietal defect, and the surgeon suddenly finds himself confronted with the need of additional sutures but is unprepared at this stage of the repair to remove free fascial strips. Such a dilemma occurred often enough that it led to more frequent use of the Gallie principle of using fascial strips taken from the lateral surface of the thigh.

Progress in the use of fascial strips is dependent not only on their intrinsic physiological and anatomical superiority in the repair of parietal defects but on mechanical refinements in obtaining them. Through cumulative experience with this technique we have devised an appliance to facilitate the removal of strips from the iliotibial tract. It does not replace the Masson stripper; rather, it complements it. Wangensteen suggested placing under the hip of the side operated upon a sand bag which elevates the thigh and gives better exposure of its lateral surface where the fascia is densest. The greater accessibility is particularly valuable when raising massive pedicled grafts. Unfortunately, this maneuver does not correct the external rotation which the thigh naturally assumes at rest or under anesthesia and which is more important than tilting the hip. To maintain internal rotation of the limb we devised a sandal (Fig. 2) in which the sole is fashioned of one-fourth inch thickness of light wood, on the bottom of which is a small metal post placed at the level of the proximal metatarsal heads to which is attached an adjustable canvas strap. This strap passes around the outer side and then across the dorsum of the inverted foot which is fastened to the opposite side of the operating table. The sandal is held securely on the foot by an elastic band which is affixed to its forepart and therefore accommodates to any size foot without impairing the circulation or producing any pressure points. We have not had a patient complain of any discomfort or after-effects from wearing the sandal. It is easily applied, simple to construct, in fact it can be made in a few minutes and of material available in any operating room. After the anesthetic is given, usually spinal, the sandal is slipped over the inverted foot with the femur rotated inward. The adjustable strap is fastened to the opposite side of the table with sufficient tautness to maintain inversion of the limb. Figures 1, 2, and 3 illustrate the mechanical sandal in use and the extraction of fascial strips with the Masson stripper. By maintaining the femur in internal rotation the stripper can be held parallel to the vertical and longitudinal planes of the thigh which enhances the smoothness with which it is passed, and there is less likelihood of tearing the strip or altering its size before reaching the desired length. Since developing the sandal we no longer place a sand bag under the hip. We belong to the school of enthusiastic believers in the superiority of living sutures and have been using the mechanical sandal more than 6 years with considerable satisfaction. The sandal is applied in every hernia repair, and the thigh is prepared routinely so that we are not delayed in the event a fascial suture is considered indicated. So far as I know there have been no other similar appliances for this purpose.

In an analysis to assess the value of the fascial suture technique in inguinal hernias we must not only compare the recurrence rate of the hernia but must include any complications arising at the donor site. In a consecutive series of 1,810 inguinal hernias operated upon in the past 5 year period (1938–1942), we have employed the Gallie repair 385 times, 321 of which were followed 1 to 5 years. In this group there were 3, or 0.9 per cent, recurrences, 3, or 0.7 per cent, infections, which persisted until the silk suture or fascial remnant was removed, 3, or 0.9 per cent, testicular atrophies, and 5, or 1.2 per cent, hematomas of the thigh which were promptly evacuated without delaying the patients' convalescence. There were no herniations through the defect in the iliotibial tract, or other complaints at the donor site. One death occurred in this series but at postmortem it was found to be unrelated to the hernioplasty.

A similar analysis of 132 McArthur repairs performed during the same period showed that there were 6, or 4.5 per cent, recurrences, 3, or 2.2 per cent, infections, no testicular atrophies, no hematomas, and no deaths.

In 1940 we (16) published follow-up studies on 457 herniorrhaphies using silk exclusively with a recurrence rate of 7.5 per cent. Therefore, it would seem from these comparative studies the fascial suture technique has a decidedly lower recurrence rate.

SUMMARY

The evolution of fascial sutures has been discussed, setting forth reasons for tardiness in their general acceptance.

The advantages and disadvantages of living sutures have been commented upon.

The importance of the Masson stripper in simplifying the procurement of multiple sutures has been emphasized.

A new foot inversion appliance consisting of an easily made mechanical sandal to facilitate the removal of fascial strips is illustrated and its use described.

A follow-up study of a series of 517 cases of inguinal hernias, repaired with autogenous fascial sutures, is submitted. The recurrence rate of 0.9 per cent (Gallie) and 4.5 per cent (McArthur) is statistical verification of their value in hernia repair. In our hands, it represents a substantial lowering of the recurrence rate as compared with other methods. We do not wish to minimize the complications. The 3 testicular atrophies and 5 hematomas occurring in this group must be taken into consideration in the final assessment of this technique. However, with increasing experience it is believed these complications can be reduced. Moreover, it should be remembered that the fascioplasty was used in recurrent and more difficult hernias occurring in patients of the fifth and sixth decades.

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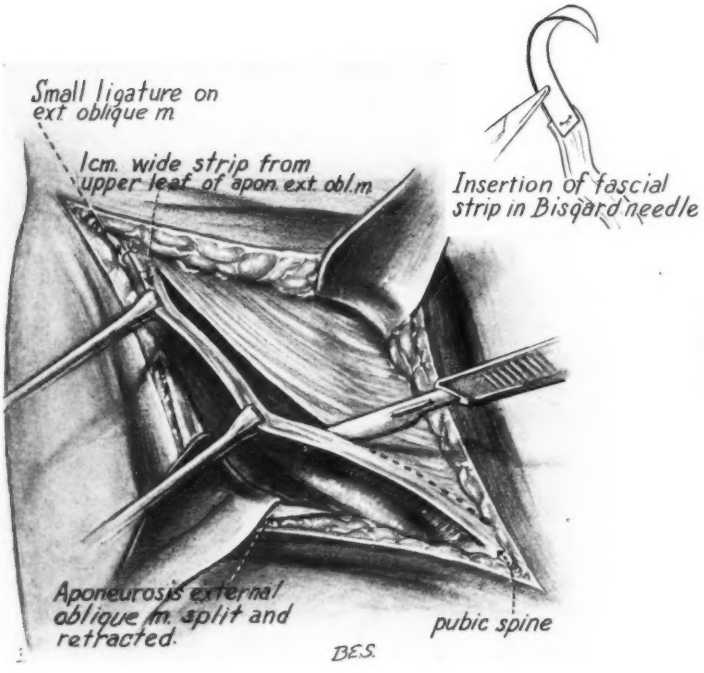
Small ligature on ext. oblique m.
1cm. wide strip from upper leaf of apon. ext. obl. m.
Insertion of fascial strip in Bisgard needle
Aponeurosis external oblique m. split and retracted.
pubic spine
B.E.S.

Fig. 2. Details of stripping the fascial suture from the upper leaf of external oblique aponeurosis. Insert shows method of anchoring the fascial suture in Bisgard's needle.

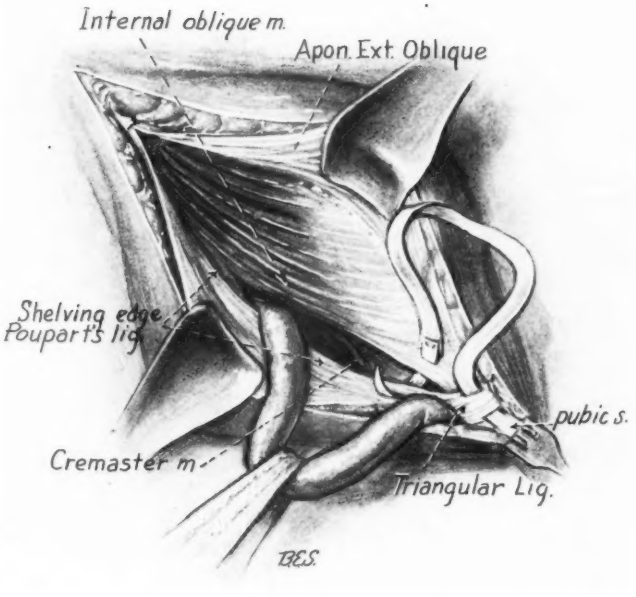

Fig. 3. This drawing shows technique of taking the first bite through the triangular ligament. (This figure should have shown the cremaster included in the continuous suture.)

LIVING FASCIAL SUTURES IN THE REPAIR OF INGUINAL HERNIA

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SINCE McArthur first advocated the use of fascial sutures in the repair of inguinal hernia, many methods for its use have been described. Unfortunately many of the methods have gotten away from the simplicity of the fundamental procedure, and a simple operative procedure has thus been made a complicated one.

Boland believes in the fundamental soundness of the Bassini technique. We agree with him but would like to add that the fundamental principle of the Halsted procedure is also sound. If to them is added the simplest method of using living fascial sutures in the main step of repair, there is evolved a simple, fundamentally sound, surgical method of repairing both direct and indirect inguinal hernia.

Roughly, about 11 per cent of all inguinal hernias are direct. Andrews believes that it is unfortunate that the term "inguinal" should group the direct and indirect types together. It is well known that a direct inguinal hernia is a simple bulging of the peritoneum and transversalis fascia into the posterior aspect of an inguinal canal which is not perfectly formed or developed. It has no relation to the cord or to the descent of the testis. It does not come through the inguinal canal. Perhaps some other term would more appropriately describe it.

Several years ago while we were teaching operative surgery at the Woman's Medical College of Pennsylvania,using human cadavers for demonstration, Dr. Alma D. Morani, my assistant, and I undertook to study the feasibility of using some simple type of operation in which successful repair could be made with living fascial sutures. The literature was reviewed and numerous methods were tried. We finally decided that a strip of fascia split off the upper leaf of the aponeurosis of the external oblique, with its lower end attached to the spine of the pubis, was the simplest and most efficacious. The use of this strip was not original with us. A Gallie needle was used in the first several cases; later, however, Bisgard devised a needle and this has since been used in all cases.

From the Department of Surgery, St. Mary's Hospital, Philadelphia, Pennsylvania.

TECHNIQUE

The operative technique must be carried out carefully in every detail. Meticulous attention to anatomy and hemostasis and careful, gentle handling of the tissues are necessary; sharp dissection is always preferable to blunt dissection and the "wiping away" of adjacent tissues. Spinal anesthesia is used in all cases unless there is some definite contraindication. The incision begins just inside the anterior superior spine and is carried down just above Poupart's ligament and over the symphysis pubis so that the upper and anterior aspects of the spine of the pubis are exposed. At this point the procedure is slowed down a bit, so that if possible, all vessels may be clamped doubly and cut between. Both sides of the incision are separated widely and retracted well. When the external oblique aponeurosis is exposed, all areolar tissue is dissected from it very carefully until the full width of the aponeurosis can be seen in the wound, as well as its full length.

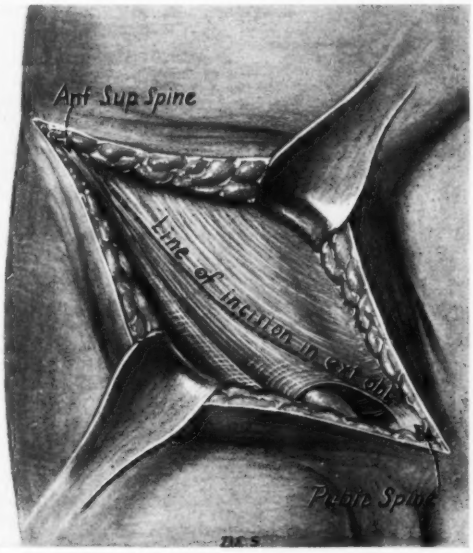

Fig. 1. Note length of incision and wide retraction exposing entire external oblique aponeurosis.

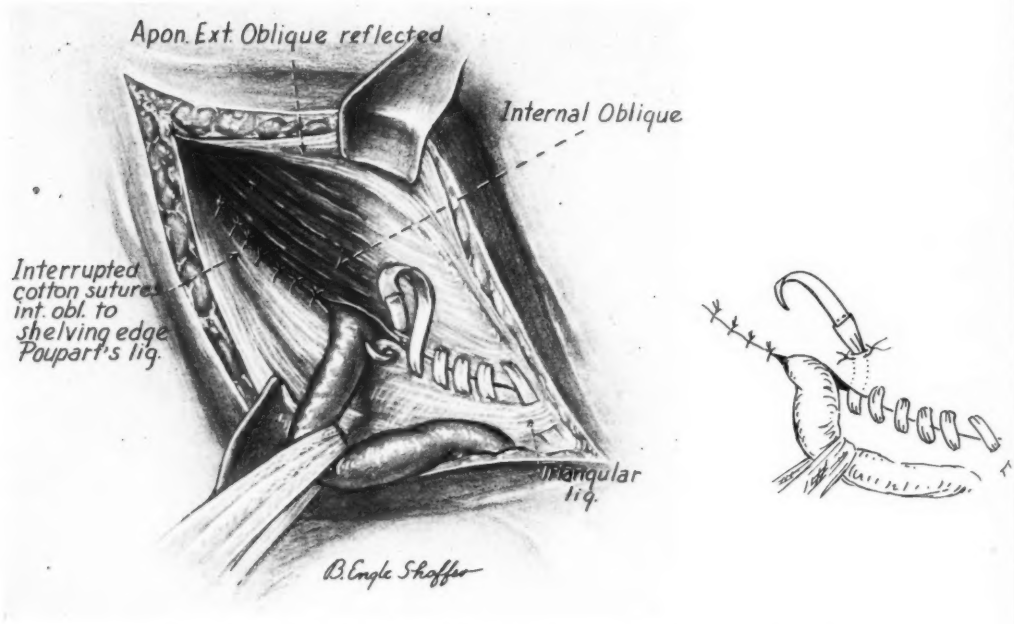
Apon. Ext. Oblique reflected
Internal Oblique
Interrupted cotton sutures int. obl. to shelving edge Poupart's lig.
Triangular lig.
B. Engle Shaffer

Fig. 4. Insert shows the anchoring of the completed fascial suture below the cord.

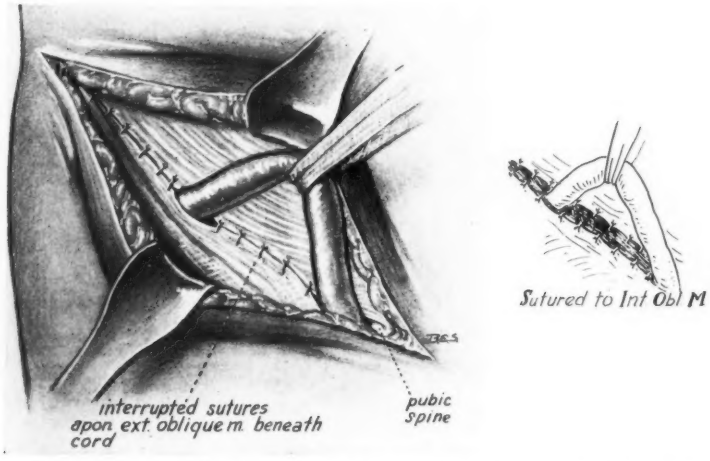

Fig. 5. Completion of the suture when the remaining aponeurosis is not under tension. Insert shows technique of suturing to the internal oblique muscle when the remaining aponeurosis is under tension.

The aponeurosis is then split at the upper margin of the external ring, the split being carried upward and outward with scissors, to the point where the aponeurosis merges into the muscle. Both upper and lower leaves are undermined to the fullest extent, and all areolar tissue is dissected from the under surface. The hernial sac is then carefully and sharply dissected from the cord, opened, its contents noted and, if possible, reduced. It is twisted several times on its long axis and tied at its base with two transfixion ligatures, the distal one about 1 centimeter from the proximal one. The ends of the distal ligature are left long. The excess sac is excised, the two ligature ends are threaded on separate needles and carried up beneath and then through the internal oblique muscle where they are tied firmly but not tightly enough to interfere with circulation. The cord is gently freed and retracted with saline moistened tapes. A strip 1 centimeter wide is split from the upper leaf of the external oblique aponeurosis beginning above and continuing down to its attachment to the spine of the pubis. Care must be taken at the upper end to ligate the muscle where the strip ends, else a hematoma will develop. The ligamentum inguinale reflexum (triangular fascia, Colles' fascia), a continuation of the lower part of the shelving edge of Poupart's ligament, is then exposed, the fascial suture is fixed in the Bisgard needle, and the first suture is carried over the pubic spine, and a good bite is taken of the ligamentum inguinale reflexum. Care must be taken to prevent twisting of the fascial suture. Then, depending on the conformation present and whether the internal oblique is broad and situated low in the wound, two methods of beginning the closure are carried out: (1) The fascial suture is carried through the shelving edge of Poupart's ligament. (2) The internal oblique muscle is picked up in the suture and then through the shelving edge of Poupart's ligament. By continuous method it approximates the internal oblique muscle and shelving edge of Poupart's ligament, including the cremaster muscle with each loop. This closes the lower angle and narrows and strengthens the inguinal triangle. This fascial suture is carried upward as high as possible to just below where the cord emerges. The fascial suture is then fixed in the belly of the internal oblique muscle by interrupted sutures. Above the cord the closure is completed with interrupted sutures. The remaining part of the upper leaf and all of the lower leaf of the external oblique aponeurosis are approximated by interrupted sutures beneath the cord. This approximation can practically always be done without tension, but in case there is tension, these two leaves are sutured down to the internal oblique muscle. The skin and fascia are then closed with interrupted sutures and Michel clips.

After operation, the patient is placed in a semirecumbent position with the knees flexed in order to relax the abdominal wall. He is kept in bed for 14 days and leaves the hospital in 16. All sutures are removed on the 7th day, following which he wears an athletic support with a wide abdominal band. On discharge from the hospital he remains in his room or on the same floor, not being permitted to use the stairs for a week. From this time on gradual resumption of walking only is permitted. If his occupation is a sedentary one, he is permitted to return to work in 1 month from the date of operation. If it is a mechanical one which requires no heavy lifting or climbing, he is permitted to return to work in 2 months. If his work is in heavy industry and requires lifting and climbing and other heavy muscular effort, he is permitted to return to work in 3 months. A careful examination, however, is made before he is permitted to return to work and then he is instructed against any sudden starts, twists, and lifts for at least 6 months.

We have carried out this procedure now in 106 inguinal hernias, 12 of which were direct. All were cases covered by workmen's compensation in which operation was agreed to by the employer or the insurance carrier. For that reason we were able to follow 92 of them back to work and to keep in touch with them. The oldest patient was 60 years of age, the youngest was 20, and all but 15 were under 40. If the patient was otherwise in good general condition we operated in all cases regardless of age. Several not in this series were supplied with supports because of poor general condition, regardless of the size or type of the hernia. There were no deaths and no serious wound complications. In 8 cases a sinus developed and discharged a suture and then cleared up. In all cases No. 30 and No. 50 black spool cotton was the only suture material and ligature material which was used except for the Michel clips in the skin.

SUMMARY

1. We believe that living fascial sutures used in the simple method described should have further trial in the repair of inguinal hernias.

2. Patients engaged in active physical occupations requiring climbing and lifting should not be permitted to return to work for 3 months after operation.

3. Ninety-two of 106 patients have been followed back to their work, and up to date we have

not been able to demonstrate any recurrences in these 92 patients. The most recent operation in this series was performed 6 months ago.

NOTE.—While we were gradually gathering this group of cases, McCloskey and Lehman (*Ann. Surg.*, 1940, 111: 610) reported a series using practically the same procedure.

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PREGNANCY IN THE MONKEY AFTER REMOVAL OF THE FETUS

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PREGNANCY is defined as the condition of the mother after conception and before birth of the child. Generally speaking, the idea of pregnancy assumes the continued presence of a developing embryo. Perhaps this has been so because death of the human fetus usually is followed by spontaneous emptying of the uterus, although this need not be a precipitate event (Streeter). The experiments with monkeys described here bring out the fact that *pregnancy, in terms of the altered maternal physiology, can be independent of the presence of the fetus for the greater part of its length.* Also, during these later months of gestation in the monkey the relative importance of the rôle of the placenta as an organ of internal secretion is emphasized and a second phenomenon, the onset of labor, is shown to be unquestionably independent of the immediate presence of the fetus.

Halban in 1905, from clinical observation alone, fully described the influence of the placenta on both the fetal and the maternal organisms. He pointed out that gravidity changes in the uterus when tubal gestation was present indicated that the placenta effected these changes through the blood stream and therefore was an organ of internal secretion. The term hormone was not yet in use. Halban stated that the source of the substances causing the pregnancy reaction was in the chorionic epithelium and observed that after early abortion of the fetus alone, or when a mole was present, growth of the uterus continued and lactation was held in check.

Since the introduction of hormone assay methods, quantitative evidence of endocrine activity of the isolated placenta has been obtained by Frank (1929) in a case in which the placenta remained in the uterus 18 days following delivery. In a study of an abdominal pregnancy after a term fetus had been removed and while of necessity the placenta had been left attached to the viscera, Ware and Main (1934) showed that the patient remained physiologically pregnant for over a month following removal of the baby. At the end of that time the urine assays became negative and the placenta presumably had degenerated.

The first experimental work in which feto-placental dissociation was accomplished was mainly concerned with growth of the mammary gland and lactation. Using the rabbit Weymeersch (1912) demonstrated that placentae persisted for some time in the uterus after the embryos were removed; and Hammond (8, 16) in 1914, observed that once started, placentae of rabbit fetuses which had atrophied at an early stage during development, persisted in some cases during the whole course of gestation. Although much smaller in size they were found toward the end of gestation attached to the uterine wall between the sites of implantations of living fetuses. The rabbit in spite of these early observations was found to be an unfavorable animal in which to study placental retention after experimental destruction of fetuses. It has been noted by Hammond and many times experienced in our laboratory (16) that in rabbits which had been subjected to operation, isolated placentae soon became detached from the wall and were expelled or later found in the uterine cavity during which time the signs of pregnancy diminished at irregular intervals after operation.

In the mouse the rôle of the placenta has been extensively studied (Newton, 1, 12, 13). In this animal the placenta survives destruction of that part of the developing ovum representing the future individual, and mice with retained placentae may, therefore, be used for comparison with those in which the uteri have been completely evacuated in the course of pregnancy. Such comparison shows that several of the maternal phenomena associated with pregnancy are determined by the presence of placentae. Thus estrus is suppressed, though it follows immediately upon total removal of the products of conception; body weight is maintained instead of abruptly falling and full mammary development

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An abstract of this work appeared in the Am. J. Physiol., 1940, 129: 485.

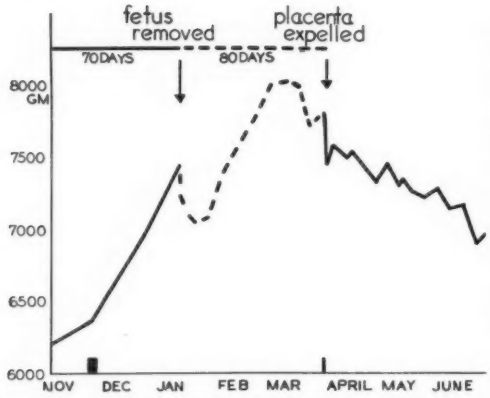

Fig. 1. Monkey C, body weight curve from day of conception through pregnancy and postpartum weight loss. The broken line indicates the time after removal of the fetus when only the placenta remained in the uterus.

occurs instead of rapid involution. The os pubis undergoes bony resorption so that the symphysis is replaced by a ligamentous structure as described in normal pregnancy by Gardner. Kirsch has confirmed these observations on the rat.

Data from the observation of other animals, while not so complete, furnish confirmation that the presence of living placentae in the uterus exerts a marked physiological effect on the maternal organism. Courrier and Gros have accomplished growth of independent placental tissue in the cat for 3 weeks, during which time the uterus remained hypertrophied. In the rat, Klein showed that suppression of estrus and the mucification of the vaginal wall depended on the placenta without the presence of the fetus. In the rat, also, Selye, Collip and Thomson demonstrated that the life span of the placenta was not markedly influenced by the removal of embryos and that the mammary glands continued development.

EXPERIMENTAL

The following experiments delineate the circumstances of fetoplacental dissociation even more distinctly, because the study has been carried out on a primate animal in which the anatomy of the genital tract and the physiology of reproduction are similar to human anatomy and physiology. More particularly, this monkey (Macaca mulatta) has a menstrual cycle of 28 days rather than the estrus cycle and the period of gestation covers six 28-day months (168 days) thus allowing such events as surgical procedures and parturition to be separated by a sufficient interval of time to establish their independence of each other.

Twelve pregnancies of 11 monkeys, all of which previously had carried babies to term, were included in these experiments. In our colony, animals customarily are mated for 48 hours during the midcycle and when pregnancy is determined, day 13 or the day nearest the 13th day of that particular menstrual cycle is counted as the first day of the pregnancy. From these animals fetuses were removed at different times, as early as the 70th day and as late as the 157th day after conception. Data concerning all pregnancies (eleven) in which the placenta was retained in the uterus after the removal of the fetus are presented in Table I. In 1 of the 12 pregnancies the placenta separated from the uterine wall during the operation, and complete evacuation of the uterus became necessary.

For success in the procedure of removing the fetus but leaving the placenta in place one point is apparently important: care must be taken not to cut the edge of the placenta. The operation can be described simply. A midline abdominal incision is made large enough to permit delivery of the uterus, following which palpation of that organ discloses the position of the bidiscoidal placenta. A generous uterine incision is made between the two placental lobes. The fetus is then lifted from the uterus, and the cord doubly ligated and cut. The placental end of the cord is dropped back into the amniotic cavity and the uterine incision closed with a single, subperitoneal, continuous suture of catgut. Delays in procedure must be avoided because handling of the uterus and section of the uterine musculature causes uterine contraction which, in the earlier months of gestation, masks the placental position.

In Figure 1 the events modifying the growth curve for monkey C are noted and the time covered is indicated by months. In this animal a male fetus weighing 50 grams was removed on the 70th day of pregnancy, following which the placenta remained in the uterus for 80 days. On the 151st day the placenta was spontaneously expelled. This was 17 days before the estimated day of delivery but only 7 days earlier than the time of delivery of a normal baby in the preceding gestation of this animal. In a multiparous animal early delivery is not unusual. The drop in weight at time of operation was from 7,450 to 7,235 grams and most of this decrease was accounted for by the weight of the fetus and the loss of blood with amniotic fluid. In this animal, as in most, there was also a further loss of weight during the ensuing week due to dehydration,

TABLE I.—DURATION OF PLACENTAL RETENTION IN RELATION TO INTERVAL BEFORE REMOVAL OF FETUS AND TOTAL LENGTH OF PREGNANCY

Monkey pregnancies	Length of pregnancy before fetus was removed	Weight of fetus	Time placenta was retained in uterus	Total number of days before expulsion of placenta
	days	grams	days	days
C	70	30	80	150
D	73*	44	90	163
B	73	50	82	155
F	99	192	70	169
J	99†	135	48	147
K	99†	142	15	114
A	100	128	84	184
E	100*	156	57	157
I	126	302	27	153
H	139	400	15	154
G	157	411	13	170

*Both ovaries removed.
†Corpus luteum removed.

trauma, and interference with feeding habits incident to the anesthetic and abdominohysterotomy.

The interesting part of the curve presented here is the resumption of the weight gain ordinarily coincident with pregnancy. The segment showing weight increment during the second half of this pregnancy parallels the pitch of the curve during the early part of pregnancy while the fetus was present. In other words, after recovery from the hysterotomy the afetal animal carried on with the pregnancy not in *status quo*, but with the pregnancy proceeding in respect to weight increment much as it would have under normally pregnant conditions. Other characteristics of the pregnancy habitus were also continued; the sex skin color heightened, and the generalized edema and the physical inactivity of the pregnant monkey together gave the outward appearance of sustained pregnancy.

Labor under these unusual conditions consists of what may be considered only the first and third stages. The signs of impending delivery are not different from usual, the animal walks about the cage, at intervals taking a sitting position on the board with hands and feet gripping the wire immediately in front of her. Strong uterine contractions can be palpated. The animal usually grasps the placenta as it appears in the vaginal orifice and makes an effort to retain and to eat it.

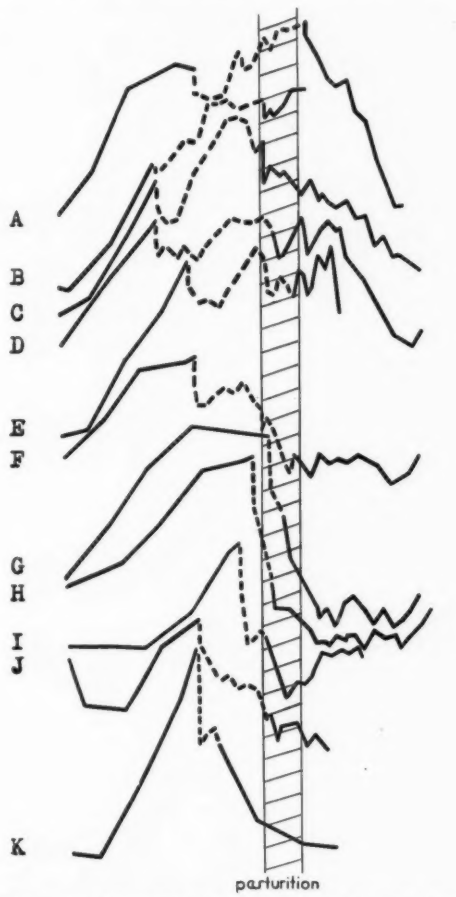

Fig. 2. Weight curves of all animals from which the fetus alone was removed during pregnancy. Broken line indicates the period during which the placenta remained in the uterus. Note that in all but the last curve this period extends into the time zone when normal end of pregnancy is expected.

Whether or not the length of labor is shortened in these cases cannot be definitely stated, but our impression is that it is not markedly sluggish or prolonged.

In the weight curve for monkey C the immediate antepartum weight loss is typical of the normal animal and the postpartum weight curve shows the usual descent. The weight taken the day before delivery of the placenta was 7,820 grams and when the animal was weighed at the time she was caught to obtain the placenta it had fallen to 7,440 grams. This drop is, of course,

much less than the usual weight change before and after delivery of a normal sized baby.

On the abscissa two periods of vaginal bleeding are shown. The first occurred 21 days after the day of conception, giving a cycle length of 32 days. The conception cycle is slightly longer than the unfertile cycles and the bleeding after conception has been called the placental sign (9). A short bleeding in early April followed the separation of the placenta. With the exception of monkey A all the other animals had a longer period of bleeding at the time of placental delivery with a normal lochial discharge.

The main points of the analysis of the growth curve for monkey C are for the most part true of the curves for all the animals which are assembled in Figure 2. In this chart the broken line represents the weight curves during the time after removal of the fetus and before expulsion of the placenta. The latticed column indicates the span of time between the 147th day and 182nd day after conception. Within these limits all the viable babies of our colony have been born. The first six records show the resumption of weight gain after recovery from laparotomy. Monkeys G and H were operated upon so late in gestation, the 157th and 139th days, that antepartum weight loss was probably imposed before recovery from laparotomy. This may be the reason for the similar reaction of monkey I. It will be seen that with one exception (pregnancy K) the broken line of placental retention extends into the zone which indicates an appropriate time for the birth of a living baby.

The length of time the placenta remained *in utero* was in direct ratio to the length of time between fetus removal and estimated parturition. Thus the placenta was retained 80 days and 90 days in instances in which the fetus was removed on the 70th and 73rd days of pregnancy and when the fetus was removed on the 157th day of pregnancy it was expelled 13 days later.

In monkey K the placental lobe lying on the anterior uterine wall was cut into inadvertently and, although complete separation was avoided, it is possible that a retroplacental hematoma formed which accounted for the interruption of pregnancy at 114 days with but 15 days of placental retention. This animal readily became pregnant again and the history of the second pregnancy (D in Table I and Fig. 2) shows removal of fetus at 99 days with retention of the placenta for 70 days and delivery occurring a single day later than the day estimated as the end of pregnancy. This was the only duplication of pregnancy in the series.

In seeking the factors ultimately concerned in the duration of pregnancy and onset of labor it was necessary to check the dispensability of the corpus luteum of gestation and the ovaries in this new situation of fetal absence. In woman and in the normally pregnant monkey (9) the corpus luteum is apparently essential only for the implantation and early development of the ovum, while in rats and mice the ovaries are necessary throughout gestation. In our experiments the ovary containing the corpus luteum of gestation was removed at the time the fetus was taken away in the pregnancies J and K, and both ovaries were removed in pregnancies D and E.

In Table I the data concerning pregnancy and operation for the 11 pregnancies are assembled and so arranged that the animal operated upon earliest in gestation appears first. It follows in general that the fetus and placenta increase in size as the fetuses are allowed longer residence *in utero*.

A correlated investigation by one of us (17, 18) has yielded further evidence of a sustained habitus of pregnancy, for it was found that the "physiological hydroureter of pregnancy" can be demonstrated by intravenous urography to persist and even to appear after removal of the fetus when the placenta remained *in utero* and functional.

In a second parallel investigation (3), assays of urine of the animals participating in the experiments reported here, indicated that the increased excretion of estrogens and androgens characteristic of pregnancy were continued throughout the time of placental retention. Following expulsion of the placenta alone, the estrogens immediately decreased to nonpregnant levels, while the high concentration of androgens persisted for a month postpartum, as was the case after normal parturition.

ANALYSIS OF STUDY

When the umbilical cord is cut and the fetus removed the active circulation of blood through the placenta is abruptly stopped. It is surprising that such a procedure, particularly when it is necessary first to cut through the uterine musculature, is not followed by immediate and effective contraction of the uterus and expulsion of the placenta.

As is demonstrated in the experimental work presented here, the monkey without a fetus remains in a condition of physiological pregnancy. Certain facts point to this being something more than a *status quo*, such as later resumption of weight increase and the appearance of ureteral

distention in late pregnancy. On the other hand, apparently lactation did not always follow expulsion of the placenta. This point could not be demonstrated with the clarity to be hoped for because the influence of suckling young was absent and because some secretion is continuously present in certain animals when they are bred year after year. Certain it is that simple removal of the fetus does not bring about lactation even when the procedure is carried out in the last month of pregnancy. The fetal surface of the placenta which has been deprived of the fetus is pale and atrophic.

SUMMARY

Fetuses have been removed from 11 rhesus monkeys and the placentae left attached to the uterine wall, and functional. The placenta remained in the uterus for the normal duration of pregnancy (defined as a time compatible with the expectation of a viable baby). Onset of labor and delivery of the placenta were normal. The placenta was spontaneously expelled after remaining in the uterus as long as 3 months in the abscence of the fetus.

During the time of placental retention the animal remained physiologically pregnant as illustrated by the several lines of evidence here presented. The most striking of these was the fact that the growth curve, after a temporary break due to removal of the weight of fetus and dehydration of operative interference, showed a progressive increase in weight which paralleled the weight-increment value in the first half of pregnancy. The usual postpartum weight loss followed delivery of the placenta.

The animals continued pregnant in appearance because of the intensification of the sex skin color, the continued presence of the generalized edema, and characteristic physical inactivity.

The length of placental retention was in direct ratio to the length of time between fetus removal and estimated end of pregnancy.

The timely onset of labor in these animals was shown to be independent not only of the immediate presence of the fetus, but also of the corpus luteum of gestation and the presence of both ovaries.

Lactation which usually follows emptying of the uterus was held in check as long as the placenta was present, but did not always follow delivery of the placenta.

Two correlated investigations furnished further evidence of physiological pregnancy in these animals. First (18), the hydroureter commonly found in late pregnancy was seen to persist until expulsion of the placenta, when it decreased abruptly. Second (3), urine assays made during the 3 periods into which this study is divided—normal pregnancy, placental retention, and the postpartum period—indicated that the increased excretion of estrogens and androgens characteristic of pregnancy were continued throughout the time of placental retention after which the usual postpartum drop of the estrogens to nonpregnant levels occurred. The androgens, as was found to be the case in the normal animal, decreased after the postpartum month of adrenal adjustment.

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PYOGENIC SEPSIS

A Survey of 255 Cases

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IN 1934 an analysis was made of 150 cases of septicemia due to pyogenic bacteria.[1] Its purpose was to elicit data which would aid in earlier diagnosis and which would suggest therapeutic procedures that might bring about a reduction in mortality. The study revealed that too much emphasis was placed on blood cultures and too little upon clinical criteria. It also pointed out various questionable aspects of some rather generally held beliefs. In addition, evidence was advanced to show that suppurative phlebitis of a substantial vein was a not uncommon cause of pyogenic sepsis. Furthermore the lesion was frequently situated in accessible venous trunks, and its surgical eradication, when feasible, was advocated.

Pyogenic sepsis appears to have received no extended attention in the intervening years, and interest in the subject today appears to be based chiefly on the results obtained by chemotherapy. Although this great advance in the treatment of septicemia, which has reduced the death rate appreciably, now overshadows other considerations, the mortality is still high. Hence it is important to learn what advances can be made in other directions. A particular reason for re-evaluating the subject at the present time is that septicemia is the most important complication of infected war wounds, especially of the extremities. In order to relate the results of chemotherapy to the problem as well as to compare the problem of pyogenic sepsis today with that of a decade ago, the cases at Mt. Sinai Hospital since 1934 are analyzed herein and are compared with the original series.

By pyogenic septicemia or sepsis is meant a clinically recognizable septic state in which an organism (usually pyogenic) can be cultured from the blood stream. The records from January 1, 1934, to December 31, 1942, were examined. All cases with positive blood culture were scrutinized and 255 satisfactorily documented cases were found. In all, a collection of pus or a phlegmonous infection was found in one or more tissues of the body. The original suppurative focus usually produced clinical manifestations but in a few instances it was found only at postmortem examination.

On the basis of the foregoing definition of pyogenic sepsis, there were excluded cases of transient bacteriemia without abscess formation occurring during genitourinary infections or following surgical procedures on the urinary tract, and cases of "cholangitis" and of "enteritis" (in infancy). Pharyngeal infections with positive blood cultures were excluded unless there was a purulent collection in the pharynx, in the adjacent cervical nodes, or in a more distant (metastatic) focus. Terminal bacteriemias were not included even in the presence of a suppurative feeding focus. Suppurative pylephlebitis is characterized by the clinical picture of septicemia but, for uniformity, all cases of infection draining into the portal system have been excluded unless attended by positive blood culture. Diseases in which nonpyogenic bacteriemia exists, such as subacute bacterial endocarditis, typhoid fever, and pneumococcemia (without pus formation), were also omitted.

More than one positive blood culture was obtained in most of the cases in this series. The absence of a subsequent positive blood culture in the balance of the cases was usually due to the rapid effect of adequate therapy. The cases in this latter small group all presented the clinical manifestations of septicemia. Thus the absence of additional positive cultures did not mean that there had existed a transient bacteriemia without clinical significance.

In the study of the records for cases of pyogenic sepsis (with positive blood cultures), cases of clinical septicemia with negative blood cultures were also investigated. A few cases were found but often the negative findings were based either on too few blood cultures or on inadequate amounts of blood obtained for culture. These cases have been excluded because they were too few in number for analysis, and their inclusion in this study would not have influenced in any material way the statistical data which is to be set forth.

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[1] Neuhof, Hirshfeld, Aufses. Surg. Gynec. Obst., 1934, 58: 886.

TABLE I.—ORIGIN OF SEPSIS

	No. cases	Incidence per cent	Incidence 1934 series per cent
Otitis, mastoiditis, lateral sinus or jugular bulb phlebitis	55	21	19
Subcutaneous abscesses, carbuncles, cellulitis	49	19	19
Osteomyelitis, suppurative arthritis	35	14	24
Postoperative	24	9	7
Genitourinary	17	7	1
Paranasal sinuses	16	6	1
Liver and gall bladder	11	4	7
Miscellaneous			
Traumatic	9		
Pharyngitis, tonsillitis	6		
Appendiceal abscess	6		
Postpartum and postabortion	6		
Lung abscess	6		
Peritonitis	5		
Traumatic phlebitis (Intravenous medication)	5		
Undetermined	4		
Pneumonia	1		
		19	
Total	255		

TABLE II.—MORTALITY IN RELATION TO CHILLS

	No. cases	Mortality per cent	Mortality 1934 series per cent
No chills	125	47	62
One chill	22	59	77
Two or three chills	43	58	70
More than three chills	65	64	68
Combined mortality of cases with chills		61	72

TABLE III.—CHILLS—THEIR INCIDENCE IN RELATION TO THE ORIGIN OF SEPSIS

	Incidence per cent	Incidence 1934 series per cent
Occurred in 130 cases	51	46
Otitis, mastoiditis etc	47	55
Abscesses, carbuncles, cellulitis	59	32
Osteomyelitis, suppurative arthritis	40	33
Postoperative	50	45
Paranasal sinuses	44	
Genitourinary	76	
Liver and gall bladder	82	90
Miscellaneous	43	43
Cases with acute endocarditis	60	43
Cases with proved phlebitis (excluding lateral sinus)	65	63

In the analysis of the cases in this series, the classifications used in the original series of 150 cases are employed whenever possible. This permits a precise comparison of the two series. Wherever the tables are comparable, the figures from the first group of cases are added.

Yearly distribution of cases (*Table XV*). With the exception of the 2 years 1935 and 1936, the number of cases yearly ranged between 35 and 45 up to 1940, when a decline began which reached a low of 11 cases in 1942. This marked decrease in the last 2 years is probably due to the widespread use of the sulfonamides in presepticemic conditions.

Origin of sepsis (*Table I*). At times an arbitrary classification of the cases in respect to the focus from which the bacteria found entrance into the blood stream appeared warranted. For instance, of the 35 cases listed under osteomyelitis and suppurative arthritis, at least 10 had had a previous history of a boil or furuncle comprising the probable primary portal of entry. However, the clinical manifestation at the time of the septicemia being referable to the osseous or articular focus, the cases were placed in that group. Similarly a number of cases in the genitourinary group comprised renal and perirenal abscesses which presumably were derived, via the blood stream, from a superficial focus of infection.

In the miscellaneous group, cases listed under pharyngitis and tonsillitis as the point of origin were those in which the throat infection played a distinct and significant part in the onset of the septicemia. Among the cases listed as peritonitis, there was some other portal of entry but the peritoneal infection was the outstanding feature in the clinical picture. Although there was usually an associated infection of paranasal sinuses and adjacent bones, such instances were not included in the osteomyelitis group, which was limited almost entirely to the long bones and vertebrae. The 4 cases in which the origin of the sepsis could not be determined clinically were all carefully examined at postmortem examination, but the primary focus could not be discovered.

More than one-half of all the cases fall in the three largest groups: mastoiditis, abscess or carbuncle, and osteomyelitis. The only significant variations from the first series are a decrease in the relative number of cases of osteomyelitis and an increase in cases of infection of paranasal sinuses and of the genitourinary tract.

Chills (*Tables II and III*). The results of the study of the present series are essentially the same as regards chills as are those of the first series. Despite a widely held impression, chills do not occur in the great majority of the cases of sepsis. They were present in only half of all cases. Furthermore neither the presence nor the absence of chills appears to constitute a significant factor in prognosis. The mortality rate was 47 per cent in cases without chills and 61 per cent in the presence of chills. As can be seen in Table III, the relative

TABLE IV.—MORTALITY IN RELATION TO TYPE OF FEVER

	Type of fever		
	Low	Elevated	Spiking
No. cases	19	73	163
Incidence—per cent	7	29	64
Incidence 1934 series* per cent	3	39	44
Mortality—per cent	58	70	47
Mortality 1934 series—per cent	50	76	63

*Twenty-one cases in the 1934 series were classified as having an irregular temperature curve.

incidence of chills, not only in the entire series but also in the individual groups, runs parallel to the 1934 series. The somewhat lower mortality of the present series (Table II) is to be regarded as the general lowered mortality in this series as compared with the earlier one. (The present mortality rate is 54.5% as compared with the previous one of 67%.)

The only marked differences between the two series in Table III the increased incidence of chills in the abscess-carbuncle group and in cases of proved acute vegetative endocarditis.

TABLE V.—BACTERIA CAUSING SEPSIS AND THEIR INCIDENCE

	No. cases	Incidence per cent	Incidence 1934 series per cent
Staphylococcus aureus	93	36.5	34
Streptococcus hemolyticus	92	36	42
Bacillus coli	15	6	3
Pneumococcus I	2		
Pneumococcus III	6		
Pneumococcus V	2		
Pneumococcus VI B	1		
Pneumococcus XX	1		
Pneumococcus XXI	1		
Pneumococcus XXIII	1		
Pneumococcus total	14	5.5	2
Anaerobic streptococcus	9	3.5	3
Bacillus Friedlaender	6	2.5	2
Streptococcus anhemolyticus	6	2.5	7
Staphylococcus albus	4	1.5	2
Bacillus proteus	2		
Bacillus pyocyaneus	2		
Streptococcus and staphylococcus	2		
Enterococcus	2		
Salmonella aertrycke	1		
Streptococcus parvulus and staphylococcus	1		
Pestis cavae	1		
Corynebacterium xerosis	1		
Bacillus Friedlaender and Bacillus coli	1		
Staphylococcus and enterococcus	1		
Bacillus fragilis	1		
Bacillus coli and enterococcus	1		
Total	255		

TABLE VI.—RELATION OF TYPE OF ORGANISM TO TYPE OF LESION

	No. cases	Incidence per cent	Incidence 1934 series per cent
Otitis, mastoiditis, etc.	55		
Streptococcus hemolyticus	47	85	86
Pneumococcus	4	7	7
Staphylococcus aureus	2	3.5	0
Bacillus Friedlaender	1	2	0
Anaerobic streptococcus	1	2	3.5
Abscesses, carbuncles, cellulitis	49		
Staphylococcus aureus	28	57	60
Streptococcus hemolyticus	16	33	21
Anaerobic streptococcus	2	4	0
Streptococcus anhemolyticus	2	4	4
Streptococcus parvulus and staphylococcus	1	2	0
Osteomyelitis, suppurative arthritis	35		
Staphylococcus aureus	31	88	75
Streptococcus hemolyticus	2	6	20
Streptococcus and staphylococcus	2	6	0
Postoperative	24		
Streptococcus hemolyticus	6	25	63
Staphylococcus aureus	6	25	0
Staphylococcus albus	4	17	9
Bacillus coli	3	12	0
Streptococcus anhemolyticus	1	4	19
Bacillus proteus	1	4	0
Pneumococcus	1	4	0
Salmonella aertrycke	1	4	0
Bacillus fragilis	1	4	0
Parnasal sinuses	16		
Staphylococcus aureus	7	44	
Streptococcus hemolyticus	3	19	
Pneumococcus	3	19	
Anaerobic streptococcus	2	12	
Corynebacterium xerosis	1	6	
Genitourinary	17		
Staphylococcus aureus	8	47	
Bacillus coli	4	23	
Bacillus pyocyaneus	2	12	
Bacillus Friedlaender	1	6	
Enterococcus	1	6	
Bacillus coli and enterococcus	1	6	
Liver and gall bladder	11		
Bacillus coli	5	45	30
Bacillus Friedlaender	3	27	30
Staphylococcus aureus	1	9	
Anaerobic streptococcus	1	9	
Bacillus Friedlaender and Bacillus coli	1	9	

Fever (Table IV). In the first series, only 44 per cent of the cases had typical septic (spiking) temperature curves. In the present group, 64 per cent

TABLE VII.—MORTALITY IN RELATION TO LESION

	Mortality per cent	Mortality 1934 series per cent
Otitis, mastoiditis, etc.	29	38
Abscesses, carbuncles, cellulitis	59	75
Osteomyelitis, suppurative arthritis	57	58
Postoperative	62.5	72
Paranasal sinuses	75	
Genitourinary	76	
Liver and gall bladder	82	100
Miscellaneous	52	91

had such fever. It is also noteworthy, that, as before, the mortality was higher in patients with low fever than in patients with spiking temperatures. The highest mortality in both series of cases was in the group with sustained fever.

The pyogenic organisms (*Table V*). The Streptococcus hemolyticus and the Staphylococcus aureus accounted for approximately 75 per cent of the cases in both series. In the first series the streptococcus was encountered somewhat more frequently than the staphylococcus, but in the present series they are found in equal frequency. This difference between the 2 series probably is due to the widespread use of sulfanilamide in presepticemic conditions, with resultant reduction in cases of streptococcic sepsis. An analysis of the relation of the type of lesion to the causative organism shows a close parallel in both series (Table VI). The Streptococcus hemolyticus remains responsible for the great majority of cases of mastoiditis and lateral sinus thrombosis (85%) and the Staphylococcus aureus is the cause of osteomyelitis of long bones and vertebrae in 88 per cent of the cases. Staphylococcus aureus is also found in 57 per cent of abscesses and carbuncles

TABLE VIII.—MORTALITY IN RELATION TO LESION AND ITS ORGANISM

	No. cases	Mortality per cent	Mortality 1934 series per cent
Otitis, mastoiditis, etc.		29	
Streptococcus hemolyticus	47	21	36
Other organisms	8	75	
Abscesses, carbuncles, cellulitis		59	
Staphylococcus aureus	28	68	82
Streptococcus hemolyticus	16	37	66
Other organisms	5	80	
Osteomyelitis, suppurative arthritis		57	
Staphylococcus aureus	31	58	55
Other organisms	4	50	
Total	139		

TABLE IX.—MORTALITY IN RELATION TO THE NUMBER OF COLONIES IN THE BLOOD CULTURE

No. of colonies	No. cases	Mortality per cent	Mortality 1934 series per cent
1 to 5	60	48	57
6 to 25	41	59	59
26 to 99	30	67	59
100 to 199	9	100	83
200 to 500	10	80	91
Innumerable	19	79	86
No count of colonies	86	40	

whereas the Streptococcus hemolyticus is encountered in only 33 per cent of the cases in this group.

Mortality (*Tables VII, VIII*). There were 139 deaths in this series of 255 cases, a mortality of 54.5 per cent. There were 84 postmortem examinations and 10 limited examinations (head cases). In the previous series of 150 cases reported in 1934, the mortality was 67 per cent. This improvement in results is due almost exclusively to the use of chemotherapy as will be shown. The otitis-mastoiditis group had the lowest mortality; the highest was found in the liver-gall bladder group with the genitourinary and paranasal sinus infections next in order (Table VII). All groups with the exception of osteomyelitis partook of the general reduction in mortality. This will be analyzed in the discussion of the rôle of chemotherapy.

The mortality of Staphylococcus aureus sepsis was slightly lower in this series than in the previous one (61% as compared with 68%). On the other hand, there was a marked reduction in the mortality of streptococcus sepsis (37% as compared with 59%). In the present series the pneumococcus group showed a mortality of 71 per cent and the Bacillus coli group 60 per cent.

Mortality in relation to the number of colonies in the blood culture (*Table IX*). Although patients with a large number of colonies in the blood stream had a somewhat higher mortality rate than those with fewer colonies, the difference was not sufficiently great to be depended upon as a

TABLE X.—MORTALITY IN RELATION TO AGE

Years	No. cases	Mortality per cent	Mortality 1934 series per cent
0–4	28	36	80
5–9	35	26	50
10–19	54	48	36
20–29	21	43	69
30–39	18	72	81
40–49	34	68	83
50–59	38	63	90
60	27	93	87

TABLE XI.—NATURE OF LESION IN WHICH COMPLICATING ACUTE ENDOCARDITIS OCCURRED

	No. cases (Total 14)	No. cases 1934 series (Total 11)
Otitis, mastoiditis, etc.	2	3
Abscesses, carbuncles, cellulitis	2	5
Osteomyelitis, suppurative arthritis	2	1
Postoperative	3	1
Lung abscess	2	
Paranasal sinuses	1	
Traumatic phlebitis	1	1
Undetermined	1	

TABLE XII.—BACTERIA IN SEPTICEMIA WITH PROVED PHLEBITIS—EXCLUDING LATERAL SINUS

	No. cases	1934 series
Staphylococcus aureus	17	6
Streptococcus hemolyticus	9	10
Bacillus Friedlaender	3	2
Bacillus coli	3	3
Streptococcus anhemolyticus	3	7
Anaerobic streptococcus	2	2
Enterococcus	1	
Staphylococcus albus	1	1
Other organisms		2
Total	39	33

basis for making a prognosis. This corresponds to the conclusion which was reached in the first series.

Mortality in relation to age (*Table X*). Approximately 50 per cent of the patients were in the first two decades of life. This parallels the 1934 series. However, a comparison of the two series reveals a marked reduction in the mortality in the first decade and an appreciable increase between the ages of 10 and 19 years. Since there is a high percentage of cases of streptococcic sepsis in the first decade, the lowered mortality may be referable to effective chemotherapy. (Fifty-nine per cent of the cases in the first decade were due to the Streptococcus hemolyticus while for the entire series this organism accounted for only 36%.)

Acute endocarditis. The analysis of the cases encountered in the first series revealed that the clinical diagnosis of acute endocarditis developing during sepsis was frequently erroneous and the conclusion was reached that the mere assumption of the existence of endocarditis should not interfere with feasible attempts at eradication of the primary or feeding focus.

Analysis of the cases in the present series substantiates the views which were then expressed. There were 14 cases complicated by acute endocarditis which were proved by postmortem examination. The presence of acute endocarditis was suspected clinically in only 7 of the 14 cases. Indeed, in 2 of the cases, clinical notes were made within 24 hours of death, stating that endocarditis was not present.

In 7 cases acute endocarditis was suspected clinically because of the presence of cardiac murmurs, petechiae, or both. Three of these 7 cases came to postmortem examination, and an endocarditis was not disclosed in any. Thus, the clinical diagnosis of acute endocarditis was incorrect in at least one-half of the cases in which it was made, and the lesion was only suspected in 50 per cent of the cases in which autopsy proved its presence.

Although acute endocarditis is thought by many to be engrafted upon a previously diseased valve, an antecedent valvular lesion was found in only 4 of the 14 certified cases. Pericarditis was also present in 4 cases and usually was due to the rupture of a myocardial abscess. Typical petechiae were present in 6 of the cases complicated by acute endocarditis, and other skin lesions in 3. Chills were present in 9 (Table III) and the spleen was enlarged in 5.

The organisms causing acute endocarditis were chiefly the Streptococcus hemolyticus—5 cases in present series, 6 in 1934 series— and the Staphylococcus aureus—4 in present series, 6 in 1934 series —occurring with equal frequency. There was 1 case in each series caused by the streptococcus and staphylococcus; 2 in the present series and 1 in 1934 series caused by the pneumococcus; 1 each in the present series caused by the Bacillus proteus and Bacillus pestis cavae. A study of the number of colonies in the blood stream reveals that few colonies were present in about one-half of the cases. Of the 14 cases in each of the present and 1934 series, we found less than 18 colonies in 6 cases of present and 5 cases of 1934 series; 30 to 75 colonies in 3 cases of the present series; and there were innumerable colonies in 5 cases of each of the present and the 1934 series. This fact negates a rather widely held view that the presence of acute endocarditis may be postulated on the basis of a progressive increase in the number of colonies in the blood. There appears to be no causative relation between the type of the original lesion and the occurrence of acute endocarditis (Table XI).

Acute suppurative phlebitis. In 1934 we stated that many cases of septicemia are due to the presence of a suppurative phlebitis in a large caliber vein acting as a feeding focus. It was argued that the correct therapeutic approach to this type of lesion was the excision of the involved vein, when feasible. Furthermore, in the presence

TABLE XIII.—THE ORGANISMS IN CASES WITH MULTIPLE LUNG ABSCESSES

	No. cases	No. cases 1934 series
Staphylococcus aureus	27	20
Streptococcus hemolyticus	2	9
Anaerobic streptococcus	2	3
Pneumococcus III	1	
Staphylococcus and streptococcus	1	
Corynebacterium xerosis	1	
Staphylococcus albus	1	1
Other organisms	1	8
Total	36	41

of evidence of a phlebitis of an accessible vein, there is no rationale in waiting for a positive blood culture. We believed that the suppurative process should be drained and the vein bearing the phlebitic area excised. This method of surgical therapy appears to have prevented the development of septicemia in a number of cases in our experience. Excluding intracranial lesions—lateral sinus phlebitis and osteomyelitis of the cranial bones—there were 39 cases of phlebitis proved by operation or postmortem examination. The veins involved were: of the extremities, 11; portal system, 9; cervical, 6; renal, 4; cavernous sinus, 4; pulmonary, 2, and 1 each inferior vena cava, umbilical and prostatic.

The bacteria which were found in these cases with demonstrable phlebitis are shown in Table XII. Aside from a reversal in the ratio between the Streptococcus hemolyticus and the Staphylococcus aureus, they parallel the 1934 findings. As already indicated, the reduction in number of cases due to the Streptococcus hemolyticus may be due to the use of chemotherapy.

From the number of colonies found in blood cultures in cases with proved suppurative phlebitis, it is established that phlebitis may occur without massive blood stream invasion. In the present series of 39 cases and the 33 cases in the 1934 series, 1 to 15 colonies were found in 12 of the present and 11 of the 1934 series; 16 to 100 colonies in 6 of the present series; 101 to 500 in 5 of the present, 9 of the 1934 series; and innumerable colonies in 2 of the present series. Data not available in 14 of the present and 13 of the 1934 series.

Chills occurred in 65 per cent of cases with proved phlebitis (Table III). They were present in a smaller percentage (50%) of cases of lateral sinus phlebitis.

A surgical attempt to remove the involved vein was made in 13 cases. Four of these patients survived. Their recovery can be ascribed to the operative procedure. The results undoubtedly would have been better if operations for eradication of the phlebitic focus had been performed before the clinical picture of sepsis was fully established.

TABLE XIV.—MORTALITY IN RELATION TO NUMBER OF PERIPHERAL METASTATIC FOCI

			1934 series	
	No. cases	Mortality per cent	No. cases	Mortality per cent
One focus	28	46	31	61
Two foci	7	71	16	75
Three foci	9	44	9	77
Four or more foci	8	37	8	25

Peripheral metastatic foci. Metastatic foci occurring during the course of septicemia may be found in any region which is fed by the blood stream. Internally the common seats for embolic abscesses were the lungs, kidneys, and spleen. Peripheral lesions usually manifested themselves as joint infections, subcutaneous or muscle abscesses, and skin foci.

As was previously noted, the mortality was slightly lower in patients with, than in those without, peripheral metastatic foci (48% as compared with 56%). It also appears that the mortality is in inverse proportion to the number of such foci (Table XIV). In this series 52 patients (20%) presented peripheral foci, only some of which were suppurative. This contrasts with the earlier series in which 43 per cent of the patients developed peripheral foci, and probably is ascribable to chemotherapy. Only 14 per cent of the patients receiving chemotherapy developed peripheral foci whereas 25 per cent of patients not treated by chemotherapy had superficial embolic lesions.

It appears to be generally held that the staphylococcus, as compared with the streptococcus, is a much more frequent causative organism in metastatic foci. That this impression is not correct is shown in both series of cases: Streptococcus hemolyticus, 26 cases in present, 30 in 1934 series; Staphylococcus aureus, 22 cases in this, 25 in 1934 series; other organisms, 4 in this and 9 in 1934 series. Indeed, the streptococcus was found somewhat more frequently in both series as shown. In contradistinction, the staphylococcus predominates as the organism in cases with metastatic pulmonary abscesses (XIII).

Multiple pulmonary abscesses. In 36 cases in this series multiple pulmonary abscesses were found at autopsy. There were also 2 instances in which multiple abscesses of the lung were diagnosed roentgenologically and the patients recovered. The incidence of pulmonary abscesses in this series is half of that of the first series.

It is interesting to note that 33 per cent of the 36 cases had less than 25 colonies in the blood

TABLE XV.—CASES RECEIVING CHEMOTHERAPY

Year	Total no. cases	No. receiving chemotherapy	Per cent
1934	39	0	0
1935	20	0	0
1936	25	0	0
1937	36	9	25
1938	43	21	50
1939	35	20	57
1940	27	22	81
1941	19	17	90
1942	11	11	100

stream (12 cases in present series, 7 in 1934 series; 25 to 100 colonies in 6 of present and 4 of 1934 series; over 100 colonies in 12 of present and 14 of 1934 series. The number of colonies was unstated in 6 of the present and 17 of the 1934 series.) As has been previously mentioned 75 per cent were caused by the Staphylococcus aureus (Table XIII). In addition to the cases of multiple lung abscesses, there were 8 cases of solitary lung abscess occurring during the course of the sepsis. Multiple pulmonary abscesses occurring during the course of sepsis are not amenable to surgical therapy. Embolic abscesses have a tendency to perforate into the pleural cavity, and this complication must be watched for and treated surgically.

Of special import is the fact that the solitary metastatic lung abscess is amenable to surgery. The fate of the 8 cases in this series is of considerable interest. Four perforated into the pleural cavity, causing empyema. In 3, which were drained, the patients recovered. Drainage was also instituted in the 4th case but the patient succumbed to septicemia. In 2 cases, a diagnosis of lung abscess was definitely made on x-ray evidence of an infiltration which in later films showed an area of rarefaction and a fluid level. One of these abscesses subsided spontaneously and the patient was discharged as cured. The other patient was not operated upon and died of septicemia. In the 7th case, a child of 3 months, the x-ray film was characteristic of pulmonary abscess. Some time later a tension pneumothorax appeared on the same side without the development of an empyema. Following the absorption of the air from the pneumothorax, and the re-expansion of the lung, the cavity was no longer visible. In the 8th case a solitary lung abscess, unsuspected clinically, was found at postmortem examination.

TABLE XVI.—PERCENTAGE OF VARIOUS GROUPS TREATED WITH CHEMOTHERAPY

	No. cases	Received chemotherapy	Per cent
Otitis, mastoiditis, etc	55	24	44
Abscesses, carbuncles, cellulitis	49	17	35
Osteomyelitis, suppurative arthritis	35	12	34
Postoperative	24	9	37
Paranasal sinuses	16	7	44
Genitourinary	17	6	35
Liver and gall bladder	11	3	27

TABLE XVII.—EFFECT OF SULFANILAMIDE IN VARIOUS SEPTICEMIAS

Organism	No. cases	Deaths	Mortality per cent
Streptococcus hemolyticus	30	4	13
Staphylococcus aureus	7	3	43
Bacillus coli	5	2	40
Anaerobic streptococcus	3	0	
Bacillus Friedlaender	2	2	100
Bacillus proteus	1	0	
Staphylococcus aureus and parvulus	1	1	100
Streptococcus anhemolyticus	1	1	100
Staphylococcus aureus and enterococcus	1	1	100
Total	51	14	27

It is interesting to note that in 1 of the cases of solitary lung abscess with perforation and empyema, the pulmonary symptoms were the first manifestation of septicemia. Following drainage of the empyema, the septic picture continued and numerous peripheral metastatic foci appeared. It was ultimately discovered that the original focus for the blood stream infection was a phlebitis of the lateral sinus. Operation on the sinus resulted in cure.

The question as to whether the lungs act as filters for the organisms in the blood stream cannot be answered by the study of our cases. Analysis of the cases with multiple lung abscesses, peripheral metastatic foci, and acute endocarditis appears to be of little value. Of 36 patients with pulmonary lesions and 14 patients with acute endocarditis, only 4 had a pathological lesion at both sites. Of the patients with pulmonary abscesses, all but 9 had other internal or peripheral metastatic foci.

The preponderance of the Staphylococcus aureus as the causative organism in multiple lung lesions is apparently the only factor which may aid in explaining the presence of multiple pulmonary foci in some cases and their absence in others. In 38 patients with Staphylococcus aureus sepsis in whom the lungs were examined at autopsy, multiple pulmonary abscesses were found 27 times (71%). In 17 postmortem examinations on Streptococcus hemolyticus cases, multiple abscesses of the lungs were found only twice (12%). On the other hand, both organisms were found with almost the same frequency in cases with peripheral metastatic foci and acute endocarditis.

TABLE XVIII.—EFFECT OF SULFAPYRIDINE IN VARIOUS SEPTICEMIAS

Organism	No. cases	Deaths	Mortality per cent
Staphylococcus aureus	9	4	44
Streptococcus hemolyticus	1	1	100
Bacillus Friedlaender	1	1	100
Pneumococcus I	1	0	
Pneumococcus II	2	2	100
Pneumococcus III	1	1	100
Total	15	9	60

TABLE XX.—MORTALITY IN CASES TREATED BY COMBINATIONS OF VARIOUS SULFONAMIDES

Organism	No. cases	Deaths	Mortality per cent
Staphylococcus aureus	12	4	33
Streptococcus hemolyticus	5	2	40
Streptococcus anhemolyticus	2	1	50
Enterococcus	1	1	100
Bacillus coli and enterococcus	1	1	100
Bacillus fragilis	1	1	100
Total	22	10	45

The contrasting behavior of the streptococcus and the staphylococcus in the lungs may be referable to a difference in predilection or in tissue immunity or may be on a mechanical basis. Concerning the latter, it is conceivable that the clumps in the blood stream derived from the feeding focus (vein) may be substantially larger in staphylococcic than in streptococcic infections and thus are more easily arrested in the lungs.

The rôle of chemotherapy. One hundred patients in this series received chemotherapy in doses considered adequate by present day standards. A number of others received doses too small to be regarded as treated with the sulfonamides. Chemotherapy was started in 1937. Table XV shows the percentage of patients receiving chemotherapy in each year. From 25 per cent in 1937, it reached 100 per cent in 1942.

Sulfanilamide was the drug most commonly used—51 cases. Sulfapyridine was administered in 15 patients and sulfathiazole in 12. Various combinations of the sulfonamides were employed in the 22 remaining cases as follows: sulfanilamide plus sulfapyridine, 5 cases; sulfathiazole plus sulfanilamide, 5 cases; sulfathiazole plus sulfadiazene, 3 cases; sulfathiazole plus sulfapyridine, 2 cases; sulfadiazene, 2 cases; sulfanilamide plus sulfapyridine plus sulfathiazole, 2 cases, and 1 each of the following, sulfanilamide plus sulfadiazene, sulfanilamide plus sulfathiazole plus sulfadiazene, sulfanilamide plus sulfapyridine plus sulfathiazole plus sulfadiazene. Sulfanilamide was used as the sole chemotherapeutic agent in 51 cases, which is the only group sufficiently large to use as an evaluation of therapeutic effect.

The mortality in the 255 cases was 54.5 per cent. In the 100 patients receiving chemotherapy, the mortality was 38 per cent. In the 155 patients who did not receive the benefit of chemotherapy, the mortality was 65 per cent. This mortality is practically the same as in the series of 150 cases reported in 1934 (67%). It is apparent that the reduction in mortality is due almost entirely to the use of chemotherapy.

Table XVI shows the percentage of the various types of cases treated by chemotherapy. It can be seen that about the same percentage of cases in all groups received the sulfonamide drugs. The slightly higher percentage in the mastoid and paranasal sinus groups is undoubtedly due to the more frequent indication for chemotherapy because of the prevalence of the Streptococcus hemolyticus in these infections. (The great majority of the cases treated by chemotherapy occurred before the introduction of sulfathiazole and sulfadiazene.)

Fifty-one patients received sulfanilamide alone. The results of sulfanilamide therapy upon the

TABLE XIX.—EFFECT OF SULFATHIAZOLE IN VARIOUS SEPTICEMIAS

Organism	No. cases	Deaths	Mortality per cent
Staphylococcus aureus	9	4	44
Streptococcus hemolyticus	1	1	100
Bacillus Friedlaender	1	1	100
Pneumococcus I	1	0	
Pneumococcus II	2	2	100
Pneumococcus III	1	1	100
Total	15	9	60

TABLE XXI.—EFFECT OF CHEMOTHERAPY IN VARIOUS GROUPS

	No. cases	Mortality per cent
Otitis, mastoiditis, etc	55	
Without chemotherapy	31	42
With chemotherapy	24	12.5
Abscesses, carbuncles, cellulitis	49	
Without chemotherapy	32	69
With chemotherapy	17	41
Osteomyelitis, suppurative arthritis	35	
Without chemotherapy	23	69
With chemotherapy	12	33
Otitis, mastoiditis, etc., due to streptococcus hemolyticus	47	
Without chemotherapy	24	33
With chemotherapy	23	9

various organisms are analyzed in Table XVII. As is to be expected, the best results were obtained when sulfanilamide was used for Streptococcus hemolyticus septicemia. The effects of sulfapyridine, of sulfathiazole, and of various combinations of sulfonamides on the different organisms are given in Tables XVIII, XIX, and XX. Because of the small number of cases in each group it is difficult to evaluate the results. The effect of chemotherapy on the three largest groups of cases is shown in Table XXI. It appears from the analysis that although the effect of chemotherapy (in this series) is by far greatest in Streptococcus hemolyticus sepsis, it nevertheless has some effect upon other organisms. Thus in the osteomyelitis group of 35 cases, the Staphylococcus aureus was the predominating organism; but the mortality in the group in which patients were treated with chemotherapy was 33 per cent as compared with 69 per cent in the cases without chemotherapy. If a single group in which there is a high percentage of Streptococcus hemolyticus cases, such as the mastoid group, is examined (Table XXI), it will be noted that in 24 streptococcus cases without chemotherapy, there was a mortality of 33 per cent, while in 23 cases with chemotherapy the mortality was 9 per cent.

Examination of the entire series reveals that in no case was an indicated surgical procedure withheld because of the anticipated effect of chemotherapy. Various other therapeutic measures were used in addition to chemotherapy without evidence of definitive effects. One hundred and fifty-five patients received one or more transfusions. Staphylococcus antitoxin was administered in 20, erysipelas antitoxin in 7, and pneumococcus serum in 6 cases.

SUMMARY

A comparison of a series of cases of pyogenic sepsis (1934–1941) with a similar series (1929–1934), reveals that chemotherapy comprises the most important advance in therapy. Furthermore the widespread use of the sulfonamides has apparently diminished the incidence of septicemia. However, the surgical eradication of the feeding suppurative focus, when feasible, is imperative if the still existent high mortality is to be reduced. This applies particularly to a suppurative phlebitis in a surgically accessible vein. The clinical recognition and eradication of suppurative phlebitis before the advent of confirmed sepsis offers the best outlook for cure.

Analysis of the present series of cases has confirmed the conclusions drawn from the first series, many of which were and still are at variance with some generally held beliefs. They are:

1. Chills occur in only half the cases of pyogenic sepsis.
2. Chills are single or few in number in more than half of the cases in which they occur.
3. The mortality is not appreciably lower in the absence of chills.
4. The temperature is of the "spiking" type in only slightly more than 50 per cent of the cases.
5. The number of colonies in the blood culture can not be used as a basis for prognosis.
6. The correct diagnosis of acute endocarditis can seldom be made; the lesion does not necessarily develop at the site of previous disease; it may be present with relatively few colonies in the blood culture and chills, petechiae, and pustules do not always characterize its course.
7. Peripheral metastatic foci are more common in streptococcus than in staphylococcus sepsis.

Chemotherapy in conjunction with surgery directed toward the eradication of the suppurative focus is the best means for combating pyogenic septicemia. Emphasis should be placed on the necessity for appropriate surgery on a feeding suppurative focus (especially suppurative phlebitis of a venous trunk) or a metastatic focus (such as a solitary abscess of the lung) in order to reduce not only mortality but also morbidity. Suppurative phlebitis can be anticipated as the most common cause of pyogenic septicemia derived from infected war wounds of the neck and extremities.

MANUAL REMOVAL OF THE PLACENTA

L. D. ODELL, M.D., and W. F. HOVIS, M.D., Iowa City, Iowa

MANUAL removal of the placenta has long been considered a serious obstetric operation. In fact, until recently (1), the maternal mortality rate has been reported as high as 13.5 per cent (2).

At the University Hospitals, manual removal of the placenta has been approached with trepidation. However, this view was recently subjected to question after observing the benign clinical course of several patients. The following data were assembled to aid in re-evaluating the risk attending the operation.

In a total of 15,824 deliveries between July 1, 1926, and July 1, 1942, manual removal of the placenta was performed 70 times, an incidence of 0.44 per cent. Two maternal deaths (from hemorrhage) occurred in connection with the procedure (2.8 per cent). According to the standards of the American Committee on Maternal Welfare, 42 per cent of the patients in the series were febrile although only 27 per cent were required to remain in the hospital longer than the accustomed 11 postpartum days. There were 47 liveborn (67 per cent) and 23 stillborn (32 per cent) infants of which 8 were previable (11 per cent).

Two major indications for manual removal of the placenta are commonly accepted, prolongation of the third stage of labor and excessive blood loss. Prolongation of the third stage prompted manual removal of the placenta in 28 patients whose blood loss was less than 600 cubic centimeters. Thirty-four operations were indicated because of excessive blood loss (over 600 cubic centimeters) without reference to duration of placental retention. It is of interest that the subsequent morbidity rate of each group was very similar (41.0 and 44.0 per cent) suggesting that intrauterine invasion rather than excessive blood loss was the principal factor in infection. The two indications are graphically portrayed in Figure 2 where the blood loss is plotted in a frequency diagram.

Abnormalities in previous confinements (28.6 per cent), especially previous manual removal of the placenta (11.4 per cent), and complications of the present pregnancy[1] (28.5 per cent) were frequent. Prolonged labor (8.5 per cent), prolonged second stage of labor (17.4 per cent) and operative delivery (41.4 per cent) were three times more frequent than usual (see Tables I and II).

Treatment of retained placenta (5) in the clinic generally follows these lines: In the absence of bleeding, at least 2 hours are allowed to elapse before manual removal is contemplated. During this time, Credé expression under anesthesia,[2] and injection of the umbilical vein with saline (Mojon-Gabaston technique, 3) are frequently employed. If the rate of bleeding is alarming, or if the blood loss becomes excessive, manual removal is performed. If possible, the operation is accomplished upon a single invasion of the uterus and the placental bed is carefully palpated for remaining secundines before the hand is withdrawn. A hot, intrauterine douche is then employed.

It should be emphasized that it is difficult, because of variations, to define a blood loss at which interference becomes indicated. Six hundred cubic centimeters is widely accepted as the maximum of physiologic bleeding but the accoucheur might be negligent in certain cases if he failed to perform the operation before this limit was reached. Similarly, he might be unduly radical in other patients if he interfered solely on this basis.

In this series, the hot, intrauterine douche has contributed materially to promotion of efficient uterine contraction and thus to adequate hemostasis. Uterine tamponade has been necessary only once. In addition, we believe that the douche mechanically cleanses the uterine cavity of bacteria and blood clot which might act as a culture medium.

Shock from excessive blood loss is the greatest immediate danger and must be vigorously combated by all available means. Transfusion of blood may be life saving and is urgently indicated in patients whose blood loss is excessive. If blood is not available, intravenous infusion of plasma or saline solution may be employed. It should be stressed that acute secondary anemia is best treated by transfusion of blood, preferably before the classic signs of shock develop. Obviously,

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[1] Placenta previa, 10; toxemia, 6; abruptio placentae, 1; intrapartum fever, 1; cardiac failure, 1; carcinoma of the cervix, 1.

[2] It is believed that: (1) Proper employment of Credé's maneuver is difficult without anesthetization of the patient. (2) The Credé maneuver, properly performed, does not cause uterine inversion since our only case of acute puerperal inversion of the uterus among 15,824 deliveries was not associated with Credé expression.

Fig. 1. Age distribution.

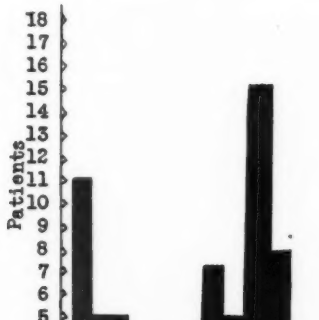

Fig. 2. Note the break at 600 to 700 cubic centimeters. To the left of the break fall those cases of prolonged third stage of labor without excessive blood loss; to the right, excessive hemorrhage. Because of emergency blood loss, measurement was impractical in 4 patients.

oxytocics should be administered to bleeding patients (See Table III).

Serious puerperal infection represents a remote danger to the patient who has recovered from the immediate emergency which may attend manual removal of the placenta, but no patient in our experience died of sepsis. It is our opinion that prophylactic sulfonamide therapy is not justified because of the relatively benign character of the infection. When puerperal sepsis occurred (44.4 per cent) the sulfa drugs were rarely indicated. They were employed only 4 times; in 2 patients who had β hemolytic streptococci and in 2 others before culture indications were recognized.

There has been a progressive decrease in mortality rates in the operation of manual removal of the placenta during the past few decades without a corresponding decrease in the frequency with which it is performed (4). The increasing use of transfusions and oxytocics, as well as more prompt interference, have undoubtedly contributed to this result.

TABLE I.—PREVIOUS OBSTETRIC COMPLICATIONS IN PATIENTS WITH MANUAL REMOVAL OF THE PLACENTA

	Patients	
	Number	Per cent
Manual removal of placenta	8	11.4
Spontaneous abortion	3	4.2
Stillbirth	3	4.2
Breech	2	2.8
Placenta previa	2	2.8
Puerperal sepsis	2	2.8
Toxemia	2	2.8
Ectopic pregnancy	1	1.4
Jaundice	1	1.4
Pyelitis	1	1.4
Uncomplicated	50	71.4

Note the high incidence of previous manual removal of the placenta. Five patients had dual complications.

TABLE II.—MANUAL REMOVAL OF THE PLACENTA, LENGTH OF LABOR, AND METHOD OF DELIVERY

	Patients		Average hospital incidence
	Number	Per cent	Per cent
Prolonged labor (30 hours or more)	6	8.5	2.8
Average labor (three to 30 hours)	57	81.4	85.7
Precipitate labor (less than 3 hours)	7	10.0	11.5
Prolonged 2d stage (more than 2 hours)	12	17.4	5.0
Prolonged 3d stage (more than 30 minutes)	50	74.2	0.61
Operative labor—total	29	41.4	11.6
Low forceps	10	14.2	6.1
Mid forceps	2	2.8	1.6
Breech delivery	9	12.8	3.6
Version and extraction	6	8.5	0.7
Craniotomy	2	2.8	

Note the higher incidence of prolonged labor, prolonged second stage and operative delivery.

Antecedent hemorrhage or infection greatly increases the danger of manual removal of the placenta. Eastman recommended that manual removal be performed before the blood loss reaches 500 cubic centimeters, while Zangemeister reported a high maternal mortality rate (18 per cent) following the operation in patients with amniotic sac infection. Procrastination during excessive bleeding is probably as radical and hazardous as interference in the presence of intrauterine infection.

The two maternal deaths which occurred in our series are briefly reviewed:

No. 40–10112 M. C., a 29 year old Mexican, quintipara, nonigravida, was admitted to the hospital in July, 1940, with a calculated date of confinement as October 10, 1940. Thirty days after admission she experienced sudden, sharp, lower abdominal pain and a hemorrhage of over 800 cubic centimeters within a few minutes. A transfusion was commenced and vaginal examination revealed placental tissue in the region of the internal os. A No. 6 Voorhees' bag was inserted, a 1 pound weight was attached, and pituitrin was administered. The bleeding, however, was not controlled and the condition of the patient became precarious. The bag was removed and re-examination disclosed a dilated cervix but no palpable placental tissue. Internal podalic version was performed without difficulty and a 3,000 gram, stillborn male infant was extracted. The placenta, which was not attached to the uterus, was immediately removed and digital examination revealed no uterine tears. A hot, intrauterine douche failed to control bleeding, and the uterus was packed. Soon after this procedure, the patient expired. No autopsy was granted.

No. 41–1559 V. C., 25 year old, secundipara, quadrigravida was admitted in February, 1941, with the expected date of confinement February 6, 1941. There was a history of edema and headaches of 2 months' duration. Examination disclosed a blood pressure of 140–100 millimeters of mercury and a trace of albumin. Following premature artificial rupture of the membranes on February 6, 1941, a 26 hour labor terminated spontaneously with the birth of a 2331 gram, living female infant. Following delivery the placenta failed to separate and numerous attempts at Credé expression were made over a 4 hour period together with repeated doses of oxytocics. The rate of bleeding, although never excessive at any time, was continuous. When the blood pressure had fallen to 70/30 millimeters of mercury and an unmeasured amount of blood had been lost, manual removal of the placenta was performed. Transfusions and other restorative measures failed and the patient expired 2 hours after the operation (6 hours after delivery).

Exitus in the first case could hardly be considered the result of manual removal of the placenta. The basic condition was fierce and uncontrolled hemorrhage resulting from abruptio placentae and it is extremely doubtful if any therapy could have saved the patient. On the other hand, the second death was a direct result of undue conservatism in the presence of continued blood loss. A fatal result might have been avoided if effective control of hemorrhage, including manual removal of the placenta, had been instituted earlier. In re-evaluating our indications for manual removal, greater emphasis will be placed upon the necessity for the operation when bleeding is continuous and prolonged, even though the rate is not excessive.

TABLE III.—MANUAL REMOVAL OF THE PLACENTA: TREATMENT

	Patients	
	Number	Per cent
Oxytocic after 3d stage	57	81.4
Intrauterine douche	49	70.0
Transfusion	33	47.1
Oxytocic before placental delivery	22	31.4
Uterine tamponade	1	1.4

Note the frequent use of intrauterine douche following manual removal. Shock was present in 19 (27.0 per cent) of our series.

SUMMARY

The experience at the University Hospitals indicates that:

1. Manual removal of the placenta does not carry the risk of infection which is usually assigned to it.

2. Failure to perform the operation in the presence of severe or continuous bleeding, or both, evidently creates a greater risk from hematogenic shock.

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EDITORIALS

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THE SANO METHOD OF ACCELERATED WOUND HEALING

THE older writers on surgery when describing methods of wound healing included "union by primary adhesion," a process that to many seemed rare or impossible and now is almost forgotten. Today we discuss wound lag and are impressed by experiments showing that five days or more elapse before the primary union of wounds really begins.

Is such lag in the reparative process essential, or is it possible deliberately to speed the processes of healing? Dr. M. E. Sano, of the laboratory for tissue culture at Temple University, Philadelphia, in a preliminary report elsewhere in this issue, suggests the possibility of eliminating "wound lag" by the use of a cement or binding substance formed of two solutions derived from normal blood. When one is painted on a split or full thickness graft, the other upon the area to be grafted, and the two surfaces apposed, almost immediate adhesion follows. Oozing of blood is arrested, and the graft is penetrated by vessels so rapidly that it acquires a reddish purple color and the edges may even bleed within 48 hours. In microscopic sections the filled blood vessels of the graft are evident early, and it soon is difficult to differentiate the graft from the underlying tissue. The procedure was the outgrowth of observations in the cultivation of embryonic tissue.

A semisolid matrix, such as fibrin, is very important for satisfactory cultivation of the living cells. Dr. Sano noted that the cell growth was tremendously accelerated when a suspension of leucocytes and the other ingredients of the buffy coat from sedimented blood was added to the culture. It seemed probable that the leucocytes have much more than a scavenger action in wound healing.

Observing the tediousness of sewing a full thickness skin graft, while assisting Dr. W. A. Steel, Dr. Sano applied her observations made during tissue culture to experimental skin grafting, in November, 1941. Full thickness skin grafts were transplanted by adhesion on rats, a suspension of the buffy coat and heparinized plasma being used. The grafts united rapidly and the experiments were successfully repeated on guinea pigs. The hair grew so luxuriantly from the graft that in a few weeks it was difficult to locate the grafted area. In September, 1942, she had her first opportunity to use the method in human practice in a grafting by Dr. W. Emory Burnett. The result was impressive, and in a recent case of his the patient was walking upon a graft on the heel within a week.

Other observations suggested that epithelization of the granulating wound about the

graft may be accelerated by applying the adhesive liquids, that sulfonamides may be combined in the process to control infection, and that grafts of tissues other than muscle, even fat—may be used in wounds to arrest bleeding. The use of the method to check hemorrhage and produce early occlusion and wound adhesion on mucous membranes is under investigation. In the peritoneal cavity a few interesting observations have been made. The bleeding surfaces of a wound of the liver promptly adhered and hemorrhage except from the margins of the wound ceased after application of the solutions. A peritoneal graft was then pasted over the area with complete arrest of the bleeding. In guinea pigs and dogs, wounds of the liver and spleen, sufficient to cause fatal hemorrhage, when painted and held together for a moment, adhered without further hemorrhage.

The possible value of such a method in treating wounds of the solid abdominal organs and in the patching of hollow viscera is an intriguing subject for additional investigation. Apparently the solutions do not produce peritoneal adhesions unless the endothelial surface is abraded sufficiently to set free cellular extractives. On the skin a large bleb may be emptied and the raised epidermis caused to readhere, and the use of the method in second degree burns immediately to produce a physiologic surface coagulum offers a possible advance in treatment.

In a few instances in which a contaminated or suppurating wound or colostomy had been cleansed and then sutured under application of the adhesives a rather unexpected primary union has followed.

The injection of such physiologic aids about ununited fractures is being compared with previous results obtained by the injection of whole blood. The relative parts played by the predominant leucocytes and of the platelets in the buffy coat remains to be better determined, as does the extent to which alien as well as pooled homologous dried blood products may be used.

In the past it has been customary to wash wounds free from the physiologic adhesives or to destroy them by soap or antiseptics. Here is a suggestion that it may be found wise to reintroduce them in concentrated form.

W. Wayne Babcock.

THE VAGINAL SMEAR IN THE DIAGNOSIS OF UTERINE CANCER

MANY women with cancer of the uterus come to the surgeon with the disease far advanced. The curability of uterine cancer would be greatly increased if the disease were recognized earlier. A simple but reliable diagnostic method would be helpful as part of a routine pelvic examination. Such a method is offered by the vaginal smear technique described and used by Dr. George N. Papanicolaou. The vagina is aspirated and the material obtained is blown on a slide which is fixed, stained, and examined. The diagnosis depends upon the recognition of tumor cells in the vaginal smear.

Papanicolaou's most recent report, *The Diagnosis of Uterine Cancer by the Vaginal Smear*[1], published with Herbert F. Traut gives ample evidence of the accuracy of this method of diagnosis. Of one hundred and twenty-seven cases of cervical cancer, a correct diagnosis by vaginal smear was made in one hundred and twenty-three. Correct vaginal smear diagnosis was made in forty-six of fifty-three cases of proved endometrial carcinoma.

It has been a satisfaction to be able to confirm, at the Massachusetts General Hospital, the excellent work of the Cornell physicians.

[1]New York: Commonwealth Fund, 1943.

We are impressed with the diagnostic accuracy of the method and believe that Papanicolaou's work should be brought to the attention of the profession.

A negative diagnosis should not be accepted as final in any patient with a suggestive history or examination. In any suspicious case a negative smear must be checked by many more slides and by examination of biopsy material. A positive diagnosis does not mean that radical surgery or radiation should be undertaken but indicates that confirmatory biopsies of the cervix or endometrium should be performed. Any patient with a positive vaginal smear who is without clinical evidence of cancer should be followed closely by repeated examinations and smears. In view of the observations made by Papanicolaou and by our group that the abnormal cells seen in these smears are actually tumor cells, great risks are assumed by any physician with extreme caution in the vaginal smear.

The ease with which material for diagnosis can be obtained by this method makes the technique adaptable to office and out-patient department practice. However, since the recognition of cancer cells in the vaginal smear requires an experienced knowledge of cytology, it is suggested that there should be in every hospital a service for the interpretation of smears, just as there is for other laboratory tests. The possibility of State Public Health Departments offering such a diagnostic service is not unreasonable.

It is my opinion that no longer can the vaginal smear be omitted from the routine examination of any female patient who is in the cancer age group.

JOE VINCENT MEIGS.

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REVIEWS OF NEW BOOKS

THE sixth volume in the series of military surgical manuals[1] published under the auspices of the National Research Council contains sections on neurosurgery and thoracic surgery. This review concerns itself with the section on neurosurgery. A number of authors have contributed to this section and presumably have been guided by the principles enunciated in the Foreword by Major General James C. Magee that "The great burden of medical care will fall on medical officers outside the highly specialized fields. It is thus essential that nearly all medical officers be familiar with the principles of military surgery"; and by Rear Admiral Ross T. McIntire, who states that "The naval medical officer is often faced with medical or surgical situations with which he must deal entirely alone and without the opportunity for consultation and assistance from other members of his profession."

The first chapter of the book, comprising 48 pages, is written by Doctors Gilbert Horrax and Claude C. Coleman on "Gunshot and Other Injuries of Scalp, Skull, and Brain." In general, it is a very practical and well organized and indexed section, and contains a reasonable number of illustrations. It will be of service to the average general military surgeon, if the latter is a person of common sense who knows his degree of competence. One might object to inclusion in it of advice such as the performance of ventriculograms, *en bloc* removal of comminuted penetrating bone over the sagittal sinus, and description of methods of electrocoagulation hemostasis in the depth of the brain. However, as stated, it may be hopefully presumed that the average military surgeon, who is not a specialist in neurosurgery, will know and respect his own limitations.

Chapter 2 on "Gunshot and Other Injuries of Spinal Cord" is written by Doctors Claude C. Coleman and Cobb Pilcher, and comprises 20 pages. It contains adequate information, which, however, might have been better organized and illustrated, considering the state of training of the men to whom it is addressed. It is the opinion of this reviewer that the average military surgeon would like to have this subject treated in a "chronological" way—that is to say, a description of immediate diagnosis and treatment, care of the patients through the various stages from the moment of the injury to the period of chronic convalescence, and descriptions of what the continued diagnostic and therapeutic measures should be. All of this information is to be found in the chapter, but the sequence in which it is presented might be confusing to a novice, unless he had mastered everything in the chapter beforehand and evolved his own philosophy from the information so acquired. Surgico-anatomical illustrations, and diagrams of tidal-drainage apparatus, etc., would have enhanced the chapter.

Chapter 3 on "Injuries of Intervertebral Disks in Military Service" by Dr. J. Grafton Love contains seven pages. It is brief and adequately illustrated and presents the problem in sufficient detail for the average military surgeon. Since these patients are almos never acutely ill, it is to be assumed, however, that this problem, which is much more complicated than is generally admitted in public speeches and writings, should be handled exclusively by specialists, either of orthopedics or neurosurgery, but usually the latter.

Chapter 4 on "Injuries of Peripheral Nerves" is by Doctors Byron Stookey and John Scarff and comprises 103 pages. This chapter is a veritable treatise on peripheral nerves and their injuries and contains a great amount of useful information—the majority of which is adequate and well illustrated. In addition, there is a supplement appearing later in the monograph, which might better have been appended to this chapter, which contains forms for examination of peripheral nerve injuries. One might say that the only, but possibly major unfavorable criticism of this chapter, is inherent in the fact that the authors have not geared the tempo of their product to the status of the recipient. The description of peripheral nerves in general and clinical examinations for injuries to them, is complete and excellent; and the description of the principles of repair falls in the same category. However, there is virtually no surgical anatomy and technique described with respect to the repair of injuries to the various individual nerves, and this, after the examination and identification of the nerve injured in a particular instance, will surely be the chief concern of the military surgeon on the field or in the general hospital.

Chapter 5 is on the subject of "Infections of Nervous System and its Coverings Arising from Injuries of War" and is written by Doctors Charles Bagley, Jr., Francis C. Grant, and Gilbert Horrax. It comprises 13 pages. The same criticisms may be applied to it as to the first chapter of the book; namely, that the information contained is good, provided the military surgeon in question knows his own limitations. There are descriptions of radical removal of infected skull requiring the use of the Gigli

[1] NEUROSURGERY AND THORACIC SURGERY. Prepared and edited by the Subcommittee on Neurosurgery and Thoracic Surgery of the Committee on Surgery of the Division of Medical Sciences of the National Research Council. Philadelphia and London: W. B. Saunders Co., 1943.

saw, complete extirpation of brain abscess, etc., which are wholly beyond the capacity of any but a neurosurgical specialist. One is distressed to note that the use of sulfathiazole powder in wounds near the brain is advocated without mentioning the precautions, which should be described, in view of the toxic and irritating effects of this particular sulfonamide preparation on nervous tissue.

All in all, it may be stated that the manual is an honest attempt by a number of recognized and experienced authors to supply the average military surgeon with a multitude of useful and easily available facts. In this, it succeeds admirably, and the reviewer does not wish to be regarded as a carping critic for having mentioned the errors of omission and commission which came to his notice. All of these may be easily corrected in subsequent editions without radical alteration of the fundamental body of the text. ERIC OLDBERG.

THE subject matter of the section of this monograph[1] dealing with surgery of the thorax "has been rigorously limited" to those special problems offered by wounds and injuries to the chest. Such general problems as the treatment of wounds in general, shock, chemotheraphy, are not discussed.

The fact that the authors have actually lived up to this idea has greatly enhanced the value of the manual from the standpoint of completely deleting all that otherwise would be repetitious when appearing in one of a series of monographs. Furthermore, it has made the manual extremely practical and readable and has greatly increased its usefulness to the civilian as well as the military surgeon. As it stands, it covers the entire subject of trauma to the chest in a clear, terse, and very understandable manner. In these days in which many general surgeons up to now have steered clear of thoracic surgery, this monograph will be of invaluable aid in bringing them up to date on procedures dealing with traumatic surgery of the chest.

The reviewer would heartily recommend that every general surgeon who has not had ample time to read much of the large literature which has sprung up relative to thoracic surgery obtain this monograph. The manual will be of value, moreover, to any physician who comes in contact with traumatic conditions of the chest, whether he be an industrial physician, a general practitioner in an isolated area where general or thoracic surgeons are not available, or even an admitting physician in a hospital.

The work is well printed, well illustrated, and the operative techniques described are standard and clearly outlined. RALPH B. BETTMAN.

NOW in a new, thoroughly revised edition, Dr. Boyd's treatise, *A Textbook of Pathology*,[2] should continue to enjoy it well deserved popularity. The motif of the book from the first edition has been the "study of pathology in relation to the living patient. It is intended to serve as an introduction to Medicine and Surgery." Dr. Boyd postulates that the "study of morphology and pathological physiology, of altered structure and disordered function, must go hand in hand, greatly to the mutual benefit of both." One but needs to read the work to see how carefully and consistently this has been followed throughout the text.

To cover the whole subject adequately in a single volume is a monumental task. However, for those who wish to supplement their reading, an excellent bibliography listing the major contributions to each subject is appended to each chapter.

The work is heartily recommended for students and practitioners. GEORGE H. COLEMAN.

THE third edition of *Blood Groups and Transfusion* by Alexander S. Wiener[3] is a rather complete revision with several entirely new sections. Perhaps the most important additions are those concerning the Rh factor. These include the story of its discovery and subsequent development, the relation of the Rh factor to erythroblastosis; a discussion of placental permeability to isoagglutinins; hereditary aspects, relationship to multiple transfusion; the technique of testing for the factor and probable subdivisions among Rh+ individuals.

Problems arising from transfusions in infants are itemized. The subjects of stored blood, plasma transfusion, and reconstituted desiccated plasma and their use in military medicine and the work of the Red Cross volunteer blood transfusion service are given. The use of blood substitutes is debated.

Geneticists will be especially pleased with this volume, for the heredity of agglutinogens A, B, M, N, Rh, the subgroups and the rarer agglutinogens is discussed fully. The portions devoted to disputed parentage and forensic medicine add a little spice and hold the attention. Racial and geographical distribution of blood agglutinogens, blood groups in disease and therapeutics bring up involved questions.

Such sections as those devoted to anthropological investigation and blood groups in animals are treated in an interesting fashion.

Of course the greater part of this book is devoted to methods and technique of drawing and administering blood, the selection of donors, transfusion reactions, their causes, prevention and treatment.

Some subjects such as the "History of Blood Transfusion" are not given completely but outstanding references are indicated in the bibliography.

For years workers in blood transfusion and blood banks have depended on former editions of Doctor Wiener's book for reference and students have found it profitable and entertaining reading. The new edition retains all of the good qualities of the old plus many new features. It is recommended to the specialist and the general reader.

CARROLL LAFLEUR BIRCH.

[1]See preceding footnote.

[2]A TEXTBOOK OF PATHOLOGY; AN INTRODUCTION TO MEDICINE. By William Boyd, M.D., LL.D., M.R.C.P., Ed. F.R.C.P. (London), Dipl. Psych., F.R.S.C. 4th ed. Philadelphia: Lea and Febiger, 1943.

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